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American Criminal Law Review
Winter, 2006

Article

*53 DATABASE LIMITATIONS ON THE EVIDENTIARY VALUE OF FORENSIC MITOCHONDRIAL DNA EVIDENCE

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ABSTRACT: Mitochondrial DNA (mtDNA) typing is increasingly being offered in criminal jury trials as proof that the defendant is a possible contributor of DNA found at a crime scene. As a prerequisite to introducing such evidence, the prosecution typically must estimate the frequency in the general population of the mtDNA sequence found in the defendant and the crime scene so that jurors can evaluate the probative value of the defendant's inclusion as a potential contributor. The government estimates sequence frequencies by comparing the observed sequence to sequences listed in a racially categorized mtDNA database developed and maintained by the Federal Bureau of Investigation and the Scientific Working Group on DNA Evidence. While mtDNA evidence has significant potential as a law enforcement tool, the SWGDAM database is currently too small and insufficiently representative to provide meaningful estimates of sequence frequencies. Most importantly, the database fails to account for historic and recent human migration patterns that, because mtDNA is maternally inherited and not recombinant, have resulted in significant regional differences in sequence frequencies. With further sampling and study, large regional databases may prove to be an effective and feasible improvement upon the current forensic database for the calculation of meaningful frequency estimates. However, until such databases and meaningful frequency estimates exist, mtDNA evidence is not yet ready for admission in criminal cases to permit inferences that suspects left mtDNA at crime scenes.

INTRODUCTION

Although the public and the legal community are now familiar with nuclear ***54** DNA, first admitted as evidence in United States courts almost twenty years ago, [FN1] nuclear DNA has a less famous counterpart found in the mitochondria of human cells, known as mitochondrial DNA ("mtDNA"). In recent years, law enforcement has increasingly used mtDNA evidence as a tool of both exclusion and inclusion of individuals as suspects in criminal cases. Specifically, because mtDNA exists in greater copy numbers per cell than nuclear DNA, mtDNA is becoming the primary type of forensic evidence extracted and reported from hair shaft samples and degraded DNA. A person may be excluded as a suspect if his mtDNA "profile," i.e., his mtDNA sequence in particular regions of his full mtDNA strand or "genome," differs from the profile of the crime scene sample. Such exclusion evidence may be relevant both at the pretrial investigation stage — to prevent wrongful accusation and conviction of innocent persons — and in post-conviction proceedings, such as Innocence Project DNA exonerations, to correct wrongful convictions. Use of mtDNA typing for exclusion purposes has been widely embraced in the scientific and legal communities because it preserves law enforcement resources by removing red herrings from investigations and focusing attention on the true perpetrator(s). [FN2]

As a tool of inclusion, however, mtDNA typing is more controversial. In criminal cases involving mtDNA, the prosecution typically reports that a defendant is included as a suspect if his mtDNA profile is consistent with, or "matches," [FN3] the profile in a crime scene sample. [FN4] Most courts also require the prosecution to present an estimate of this shared mtDNA profile's frequency in the relevant population, [FN5] on grounds that, without such an estimate, jurors cannot meaningfully assess the probative value, if any, of the defendant's inclusion as a potential ***55** contributor. To estimate such frequencies, an analyst typically compares the suspect's mtDNA profile to a forensic reference database compiled and maintained by the Scientific Working Group on DNA Evidence ("SWGDAM"), a group sponsored by the Federal Bureau of Investigation ("FBI"). [FN6] In comparing a suspect's sequence to the SWGDAM database, the analyst counts the number of times the sequence appears in various sub-databases organized by the self-reported "race" [FN7] of the sample contributors, then uses this number to estimate the true frequency of the sequence in each race-based population. [FN8] Because of the small size of these databases and the diversity of mtDNA profiles, [FN9] this approach usually yields zero "hits" in the database. Thus, the estimated frequency of the sequence reported out is often less than 0.1%. [FN10] Such a low estimate is potent evidence in a criminal jury trial because it suggests that a randomly selected individual has only a 1 in 1000 chance of sharing the profile observed in the crime scene sample.

Of course, a frequency estimate is only as good as the statistical method used to calculate it. If the method is invalid, such as if the database is not representative of the relevant population, the resulting frequency estimates may be inaccurate and, if so, will not give the jury a meaningful way to evaluate the probative value of the reported inclusion. In turn, if the probative value is unknown or inaccurately reported, most courts would rule that the evidence of inclusion is inadmissible based on rules of relevance and novel scientific evidence. Thus, whether the SWGDAM database is a valid tool to estimate mtDNA sequence frequencies is a critical question courts should ask in determining whether to admit evidence of mtDNA inclusions. Neither forensic scientists nor attorneys frequently present these questions to courts in a considered way. This Article is an attempt to ***56** encourage the legal and scientific communities to view these questions with a more critical eye.

Part I of this Article briefly discusses the fundamentals of mtDNA biology and forensic typing methods and how they differ significantly from nuclear DNA biology and typing methods. Part II explains mtDNA's forensic applications and the particular methods used by the FBI to type mtDNA sequences and estimate sequence frequencies using population databases.

Part III contends that reported mtDNA frequency estimates are currently misleading because the SWGDAM database from which the estimates are calculated is neither representative of the general population nor of the various subpopulations it professes to characterize. First, the SWGDAM database is an incomplete, non-random, non-representative collection of mtDNA profiles compiled without regard to geographic patterns of genetic clustering that have resulted from cultural, political, historical, and economic forces. Second, current reliance in criminal cases on estimates derived from comparisons to the SWGDAM database is misplaced given the poor quality control measures of the database and the manner in which the assessment method is skewed toward reporting an inclusion.

Part IV examines both the general principles governing the admissibility of scientific evidence in most jurisdictions and courts' treatment of mtDNA inclusion evidence. Part IV argues that, because the estimation of profile frequencies using the SWGDAM database is currently controversial and of questionable validity, evidence of mtDNA inclusions does not yet meet most jurisdictions' legal standards for admissibility.

The Article concludes by prescribing various measures to improve the quality and integrity of forensic mtDNA typing. It is the expectation of the authors that, once mtDNA evidence is properly understood in its full scientific context, and once statistically valid databases can place a true probative value on mtDNA evidence, it will be reliable, highly rel-

evant, and properly used in criminal investigations and prosecutions. Today, however, the state of mtDNA evidence presents an unacceptable risk of accusing or convicting the innocent based on inaccurate and misleading scientific evidence.

I. THE BASICS OF MTDNA TYPING AND HOW IT DIFFERS FROM NUCLEAR DNA TYPING

A. Differences in the Biology of MtDNA and Nuclear DNA

Deoxyribonucleic acid ("DNA") exists in every human cell and contains genetic codes inherited from previous generations. Humans have two types of DNA: nuclear DNA ("nDNA") and mtDNA. The mtDNA genome is distinct from the nDNA genome, and the two types of DNA differ in terms of their location within the body, genome size, and genetic makeup. While nDNA is bundled within chromosomes in the nucleus of most human cells, mtDNA exists outside the ***57** nucleus in energy-producing organelles called mitochondria. The mtDNA genome is also much smaller than that of nuclear DNA; while the nuclear genome consists of approximately three billion base pairs, [FN11] the mtDNA genome contains approximately 16,569 base pairs. [FN12] The mtDNA genome consists of two primary regions: a *coding region*, which regulates the production of various biological molecules, and a *control region*, which regulates replication of the mtDNA molecule itself. [FN13] The control region, approximately 1125 base pairs long, [FN14] is the only significant portion of the mtDNA strand that does not code for genes. [FN15] In contrast, the nDNA genome contains coding regions spread throughout the twenty-three chromosomes that are known to have a genetic purpose, surrounded by regions of so-called "junk" nDNA, for which scientists have yet to find a genetic purpose.

B. Differences in Forensic Typing of MtDNA and Nuclear DNA

To distinguish one individual's DNA from that of another, forensic scientists look to particular locations within noncoding regions of the nuclear and mtDNA genomes that are highly variable among humans and therefore have discriminating power. In nuclear DNA typing, scientists typically look to thirteen locations along an individual's nDNA strand identified by the FBI as particularly suitable for forensic testing and used by the FBI to generate the profiles contained in its Combined DNA Index System (CODIS). A person's forensic nDNA "profile" consists of the twenty-six alleles he exhibits at these thirteen "CODIS loci." [FN16]

To compare individuals' mtDNA strands, most forensic scientists focus on two regions within the mtDNA control region — "Hypervariable Region I" ("HVI") and "Hypervariable Region II" ("HVII") — that together encompass approximately 610 base pairs and that exhibit high mutation rates and high amounts of variation from person to person. [FN17] A person's mtDNA "profile" consists of a list of the differences in HVI and HVII between that person's sequence and a reference sequence called the Cambridge Reference Sequence ("CRS") or "Anderson sequence," so named ***58** because the mtDNA genome of a particular individual, Stephen Anderson, was completely sequenced in 1981 by biochemist Fredrick Sanger in Cambridge, England. [FN18]

Scientists have begun to sequence nucleotides other than those in HVI and HVII in an effort to provide additional means of distinguishing different individuals' mtDNA. [FN19] They have focused, for instance, on a region referred to as "Hypervariable Region III" ("HVIII"), [FN20] also in the control region. In addition, even greater discrimination may be possible by typing certain nucleotides in the coding region called Single Nucleotide Polymorphisms ("SNPs"), single locations along the mtDNA genome exhibiting hypervariability. [FN21] Most forensic analysts do not currently type these additional locations along the mtDNA genome both because they know little about the variation outside HVI and

HVII and because of convenience and cost concerns. [FN22] Exceptions exist, however; the Armed Forces DNA Identification Laboratory ("AFDIL") is currently attempting to detect levels of variation throughout the entire mtDNA genome for forensic purposes. [FN23]

MtDNA typing also differs significantly from nDNA typing because of the manner in which mtDNA is inherited. A child inherits twenty-three chromosomes from both of his parents; each set of chromosomes contains a full complement of nDNA strands with 3.2 billion base pairs. Thus, at each location along the nDNA **59** strand, each individual has two genetic forms or "alleles" — one from each parent. [FN24] Of course, the parents each have two alleles at each location as well; which one of these two alleles each parent passes on is random. At each of the thirteen locations along the human nDNA genome used in forensic testing, only a limited number of possible alleles have been observed. As recombination occurs with each successive generation, different combinations of alleles are created over time. In contrast, scientists generally believe that the human mtDNA genome is only passed on from mother to child. [FN25] Consequently, all biological children of one woman will, absent mutations, have identical mtDNA profiles, and, going back generations, *all* relatives within the maternal lineage, absent mutations, will share the same mtDNA sequence.

While mtDNA's lack of recombination makes mtDNA sequences relatively static compared to nDNA, mtDNA exhibits a high rate of mutation between generations. Some regions of mtDNA evolve at rates five to ten times faster than single-copy nuclear genes. [FN26] Consequently, while each member of a maternal line should theoretically exhibit identical mtDNA profiles, the high mutation rate of mtDNA means that the profiles of members of the same maternal line, particularly over generations, may be slightly different.

Individuals are "homoplasmic" with respect to their nuclear DNA profile, meaning that all nuclear DNA strands found in a person's body contain the identical genetic material and do not differ from cell to cell. As recently as ten years ago, most scientists considered the vast majority of individuals to be "homoplasmic" with respect to mtDNA as well. [FN27] Scientists now understand, however, that most, if not all, individuals are actually "heteroplasmic" with respect to mtDNA, meaning that an individual's mtDNA sequence can differ among **60** locations in the body, or even within the same cell. [FN28] Although heteroplasmy is routinely observed, its causes are not fully known. [FN29] The chance of detecting heteroplasmy depends on the sequencing chemistry and techniques used. [FN30] Some body tissues, such as hairs, tend to show more variability in mtDNA sequence than others. [FN31]

Heteroplasmy and high mutation rates complicate forensic mtDNA analysis in two respects. On the one hand, samples from a suspect and a crime scene may, because of heteroplasmy, exhibit mtDNA sequence differences even when the two are, in fact, from the same individual or lineage, thus leading to potentially false exclusions. On the other hand, the suspect and crime scene samples may exhibit sequence commonalities even when the two are, in fact, from different individuals.

One other important difference in the state of current nDNA and mtDNA typing is the existence of population databases from which accurate frequency estimates can be generated. Scientists have conducted many population studies to generate population frequency estimates for nDNA and have reached some agreement that, using modifications to account for population inter-relatedness, reliable frequency estimates are possible. [FN32] In stark contrast, the frequency and distribution of mtDNA sequences in the population are not yet known. These population substructure issues with respect to mtDNA are the focus of nascent, but already quite active, scholarship among genetic anthropologists and forensic scientists. [FN33]

What *is* known about the frequency of mtDNA profiles in the population suggests that, unlike nuclear DNA, mtDNA profiles are far from randomly distributed. Groups of people with similar mtDNA within a circumscribed range of vari-

ation are called "haplogroups"; variation within a haplogroup divides people into "haplotypes," or particular mtDNA sequences. Researchers have named haplogroups observed in certain populations, based on the presence of certain ***61** combinations of variations. [FN34] For example, ten mtDNA haplogroups have been identified at significant frequencies in the European and U.S. European-American sub-populations. [FN35]

II. THE USE OF FORENSIC MTDNA TESTING AS A TOOL OF INCLUSION IN CRIMINAL TRIALS

To be clear, mtDNA typing is used as a tool of identification in many fields unrelated to inculpation of suspects in criminal trials. Because mtDNA is maternally inherited and found in higher copy number than nDNA, mtDNA analysis is particularly helpful in conducting population studies for medical, [FN36] genealogical, [FN37] and anthropological purposes, [FN38] and has been used by the military to identify casualties of war and terrorism. [FN39] For example, through mtDNA analysis, scientists have been able to identify victim remains from the World Trade Center tragedy, the Oklahoma City bombing, the Bosnian War, natural disasters, and plane crashes. [FN40] The demonstrated utility of mtDNA testing in these contexts stems ***62** largely from its ability to identify maternal lines and to exclude individuals whose profiles differ from questioned samples. For similar reasons, mtDNA is appropriately used in criminal cases to exonerate persons whose mtDNA profiles are revealed inconsistent with crime scene samples. [FN41]

The FBI has led the field in the use of mtDNA evidence to *inculpate* criminal suspects. The FBI began studying mtDNA technology in 1992 and conducting mtDNA casework in 1996, [FN42] and is now one of a handful of public and private laboratories in the United States that conduct forensic mtDNA testing. [FN43] Because the FBI is the federal government's forensic laboratory, and because SWGDAM, under the auspices of the FBI, maintains the sole database used in the United States in forensic mtDNA analysis, this Article discusses its procedures as illustrative of all forensic mtDNA laboratories. What follows is a description of the FBI's methods for developing a suspect's mtDNA profile, determining whether the suspect should be "included" as a potential contributor because his profile is consistent with the evidence sample profile, and calculating the statistical significance of an inclusion through estimation of sequence frequencies in the population using the SWGDAM database. [FN44]

An analyst first sequences the HVI and HVII regions of a sample found at the crime scene. Next, assuming a suspect has been identified and has submitted a DNA sample, the analyst sequences the HVI and HVII regions of the suspect's sample and compares the two profiles against each other. The FBI, according to its protocols, does not automatically exclude a suspect if his profile differs from that of the evidence sample. Indeed, the FBI will only definitively exclude a suspect if there are two or more base pair differences between the samples with no evidence of heteroplasmy, on the theory that one difference may be the result of heteroplasmy. [FN45]

While the FBI declares an automatic exclusion only in cases involving two or more differences, the FBI will declare an *inclusion* (called a "failure to exclude") ***63** under several different scenarios. [FN46] Thus, if the examiner determines that the profiles of the suspect and evidentiary samples are identical at each of the bases in HVI and HVII, the suspect is included as a possible contributor. [FN47] The examiner also will not exclude the suspect if the profiles have a one base-pair difference and either sample displays heteroplasmy. [FN48] If the profiles have a one-base pair difference in HVI and HVII and no evidence exists that the suspect or evidence sample is heteroplasmic, the result is "inconclusive," and the suspect will again not be excluded. [FN49] As explained in Part I, the FBI does not sequence outside HVI and HVII to determine whether other differences exist besides those already observed that could exclude the suspect as a potential contributor to the evidence sample.

If the suspect's profile is consistent with the evidence profile, the analyst then compares this shared profile to the SWGDAM database. [FN50] The entire database contains 5071 profiles. [FN51] The database is subdivided into fourteen

so-called "racial" sub-populations. [FN52] The database profiles come from samples collected by **64** paternity testing laboratories, blood banks, FBI agents, and scientific research groups. [FN53] The classifications of the sequences are based on the self-reporting of the individuals who agreed to give the samples. The FBI does not claim that these samples are geographically diverse, randomly selected, or representative. Rather, the samples were obtained in an *ad hoc*, non-random manner from a few locations. [FN54]

To generate frequency estimates from the SWGDAM database, forensic scientists count the number of times that the shared profile "matches" a profile in each of the sub-population databases (the "counting method"). [FN55] The analysts count only the number of appearances of the profile in the database and not the appearances of the profile in the suspect and in the evidence sample. Because the SWGDAM database omits the vast majority of mtDNA profiles and because more than 50% of the profiles in the SWGDAM database appear only once in the database, [FN56] this approach most often results in a count of zero observations or "hits."

The analyst next estimates the rarity of the profile in various "racial" populations based on the number of observations in each of several sub-databases categorized by self-reported ancestry. If the analyst sees at least one observation, **65** this process involves dividing the number of observations by the size of the database. [FN57] For example, if the profile were observed once in the African-American database (n = 1148), the frequency would be 1/1148 or 0.0008711. The analyst would then place a 95% confidence interval around that number as a margin of error in estimating the frequency in the larger population, [FN58] and the laboratory would report the upper-bound frequency. For an observed frequency of 0.0008711, the upper confidence limit is 0.002577, or 0.2577%, and the laboratory would report that about 99.74% of African Americans are excluded as potential contributors of the sample.

Because all people sharing a common maternal lineage are expected to have the same mtDNA sequence (excluding considerations of intergenerational mutation), the FBI acknowledges that examiners cannot declare identity based on mtDNA analysis alone. Yet such small reported probabilities of inclusion calculated from the SWGDAM database can suggest to juries that the consistency between the mtDNA profiles is a "match" amounting to a statement of identity. [FN59] Based on such small frequency estimates, mtDNA evidence has thus become a powerful tool of prosecution. A closer examination suggests, however, that such frequency estimates are based on faulty scientific assumptions that do not meet prevailing legal standards for admissibility of scientific evidence, and should not, in their current state of development, be admitted against criminal defendants at trial.

III. THE DUBIOUS RELIABILITY OF FREQUENCY ESTIMATES ASSOCIATED WITH FORENSIC MTDNA

The current SWGDAM database suffers from several structural problems that make it incapable of producing reliable estimates of mtDNA profile frequencies in particular geographical and ancestral populations. *First*, the database is a statistically unsound sample set from which to estimate mtDNA sequence frequencies **66** because it does not account for geographic and ancestral clustering of identical or related mtDNA profiles. Specifically, the manner in which the samples are collected — samples taken from a handful of arbitrarily selected regions of the United States — assumes, incorrectly, that mtDNA profiles are randomly distributed in the population. But unlike nuclear DNA, which always reflects inheritance of certain of the mother's and father's unique influences and thus varies even between siblings (except identical twins), mtDNA is maternally inherited, does not recombine, and is far from randomly distributed in the population. Moreover, the "racial" categories in the databases, do not sufficiently take into account the intra- and inter-ethnic diversity resulting from well-documented ancestral migration patterns and clustering of profiles into identifiable haplogroups. *Second*, the SWGDAM database is too small in relation to the general populations it purports to represent to estimate such frequencies adequately. *Third*, even if the database were representative and large enough, significant previ-

ously unaddressed quality control problems undermine its reliability. *Fourth*, as applied, the "counting method" potentially understates frequency estimates systematically through assumptions biased against suspects. While each of these problems can be remedied, their existence suggests that reliance upon the current SWGDAM database is currently unfounded and that such issues should, in any event, be addressed by attorneys and the courts.

A. MtDNA Is Not Randomly Distributed in the Population

1. The Statistical Validity of the SWGDAM Database Is Premised on False Assumptions about the Distribution of MtDNA Profiles in the Population

Many of SWGDAM's sequences came from the same samples that existed in the FBI's STR databases used to generate match statistics in forensic nDNA typing. [FN60] In nuclear DNA testing, forensic scientists typically obtain miniscule random match probability statistics generated by comparison of alleles at each of the thirteen standard STR locations. [FN61] The nDNA STR databases, and the validation studies thereof, were based on the premise that, particularly given the miniscule associated statistics, only statistically insignificant genetic linkage exists within the populations sampled. Accordingly, for nDNA, it was concluded that sampling from a small number of locations was acceptable. [FN62]

This assumption of randomness is not valid with respect to mtDNA sequences. As explained below, because mtDNA is maternally inherited and not recombinant, ***67** mtDNA profiles are not randomly distributed. The distribution of a particular mtDNA sequence is primarily a function of the migration of women. A child and his maternal great-great-great-great-grandmother, or a child and all of his mother's sisters' children, are expected, absent mutations, to have identical mtDNA profiles. Over generations, profiles stay intact or mutate to a very similar sequence. In addition, the high mutation rates characteristic of the HVI and HVII regions create unique variants, including more recently created ones that have not had time to spread from their location of origin. This creates geographical areas where certain haplogroups or haplotypes are prevalent, and other areas where those same haplogroups and constituent haplotypes are wholly or largely nonexistent.

2. Phylogeographic Studies Confirm That MtDNA Haplogroups Exist and Are Geographically Stratified

Dozens of phylogeographic [FN63] studies have been performed to identify the geographic distribution of mtDNA haplotypes in countries all over the world, although such studies are extremely limited in the United States. These studies demonstrate that mtDNA is not randomly distributed and that different haplogroups and haplotypes are concentrated within certain populations that vary geographically. [FN64] Scientists rarely come across new nDNA gene types when studying new population subgroups; however, the same is not true for mtDNA sequences. While certain haplogroups of mtDNA sequences are widely distributed throughout the population, [FN65] many exist only within certain geographic clusters. [FN66] ***68** Non-random mtDNA haplotype distributions also exists *within* geographic locations, because of often subtle linguistic, religious, or economic/caste distinctions. [FN67]

Distinctive mtDNA haplotype distributions are not limited to rare or ancient populations; today, different geographic regions demonstrate strikingly different mtDNA patterns. [FN68] For example, a particular cluster of mtDNA sequences called haplogroup J is widely distributed in western and central Europe, but is rare in the Iberian Peninsula. [FN69] A sub-haplogroup of that cluster has been observed primarily in Britain, with one other occurrence from an ancestor in Italy. [FN70] A mutation that has an 8% frequency within the Canary Islands has never been found outside the Islands.

[FN71] One study related to the natives of Mozambique as compared to those in the Americas identified a considerable number of matches between Mozambique and American sequences from African haplogroups, including some sequences ***69** that had never been observed outside Mozambique, as well as others observed only in the American populations. [FN72] From 2000 to the present, the AFDIL has been documenting such regional differences through a DOJ-funded effort to create databases of mtDNA control region sequences for African-origin, Hispanic, and Central Asian individuals. As of July 2005, AFDIL had databased "249 African-American, 646 U.S. Hispanic, and nearly 2500 Central Asia samples." [FN73] The five-year project "is intended to ... investigate the potential for forensically significant regional variation within U.S. racial/ethnic groups" and has success-fully unearthed such significant results, particularly with respect to U.S. Hispanics. [FN74] Based on these observed differences, AFDIL reported to the National Institute of Justice that its "work establishes that there is highly significant geographic variation of mtDNA types among individuals classified as 'Hispanics' in the United States" and that "[t]his has serious implications for the appropriate structuring of forensic mtDNA population databases." [FN75] To the AFDIL researchers, "[i]t seems very unlikely that reference to a single Hispanic database can be justified in evaluating the significance of mtDNA matching in the Hispanic population." [FN76]

Similarly, a study of the Han Chinese revealed dramatic regional differences in haplogroup frequencies among a population that constitutes 93% of the Chinese population and nearly 20% of the world's population. [FN77] Researchers examined 263 unrelated Han Chinese samples taken from six different provinces. They observed that, while certain haplogroups made up almost 20% of the population in a certain province, the haplogroup was nonexistent in a different province. Ultimately, the clustering in particular provinces was so pronounced that the authors concluded that an East Asian database, or even "Northern Han" and "Southern Han" databases, would grossly underestimate the frequency of certain groups of sequences***70** that themselves are highly common in surrounding regions. [FN78]

MtDNA population genetic linkage in North America — discussed in detail in the next two sections — is also well documented in scientific research. [FN79] Whether the heterogeneous geographic distribution of mtDNA lineages reflects genetic clustering, inadequate sampling, or some combination of the two, it appears clear that the sampling of mtDNA profiles must take into account geographic heterogeneity and stratification in order to create representative databases for use in forensic typing.

3. Significant Ancestry-Related Population Substructure Exists in the Distribution of MtDNA Sequences in the African-American Population

The SWGDAM database also fails to account for ancestry-related clustering of haplogroups in the United States, particularly with respect to the collective experience of African Americans, whose post-slavery era migration patterns are well documented. [FN80] The oldest mtDNA profiles stem from Africa, whose population***71** displays great regional diversity and heterogeneity in mtDNA profiles. [FN81] In some regions, specific mtDNA profiles are common; in others, the same mtDNA profiles are rare or nonexistent. [FN82] Scientific studies in Africa repeatedly uncover more unknown and previously unexamined mtDNA sequences, and far more is left to learn about regional differences that exist both now and hundreds of years ago.

During the period of slavery in the United States, the forced migration of Africans to the New World brought these regional differences to the United States and led to significant regional differences in the ethnic and geographic ancestry of African Americans. [FN83] Various political, economic, and cultural factors associated with the implementation of slavery contributed to these regional differences. For instance, during the period of slavery in the South, plantation owners in South Carolina primarily grew rice. These owners sought West Africans who already knew how to grow rice and

therefore imported enslaved Africans from the "Grain Coast" of Africa. [FN84] In contrast, in Virginia, plantation owners primarily sought to grow tobacco. [FN85] The area surrounding the tobacco farms was swampy, and with the swamps, mosquitoes and malaria were common. [FN86] Neither Native American nor European American workers had genetic resistance to malaria and were dying in large numbers. Plantation owners sought enslaved Africans resistant to malaria and turned to the "Gold Coast" — modern day Ghana and Benin. [FN87] Similarly, because ***72** Portuguese and French slave traders were the primary slave traffickers in New Orleans, many of the enslaved Africans brought to Louisiana were from Angola. [FN88] Thus, the forced migration of enslaved Africans to the United States led to geographic variation in this country similar to that of regional African variation.

Once in the United States, the clusters of African Americans either remained in their geographical origins or migrated in distinct groups, as family members joined family members, friends followed friends, and neighbors encouraged neighbors to emigrate. [FN89] This patterned migration resulted in further geographic variation throughout the United States. For the most part, this took place during the "Great Migration" — roughly 1910 to 1930 — when African Americans in the rural south traveled north for better jobs in light of World War I and a boll weevil crop infestation in the South. [FN90] These migrations took predictable routes: African Americans from Mississippi, Alabama, and Louisiana largely followed the Mississippi River and migrated to the great cities of the Midwest, such as Detroit, Chicago, Cleveland, and Kansas City; and African Americans from the Carolinas and Virginia tended to travel up the coastline to Washington, D.C., Philadelphia, and New York. [FN91] Notwithstanding the effects of this large-scale migration, most African Americans have remained in the southern part of the United States, in the crescent-shaped region ranging from Washington, D.C. to Louisiana. [FN92] Today, scientists observe genetic variation among African Americans in different regions of the country based upon the routes of those African Americans who migrated there and based on the variable levels of mixing with European Americans in different parts of the United States.

Heterogeneity also exists in African-American mtDNA profiles as one moves westward across the country. African Americans living in the western United States tend to exhibit larger percentages of European and Native American ancestry than those living in the South, Mid-Atlantic, and Midwest. [FN93] These phenomena may be the result of history, in that western territories and states had less restrictive social mores with respect to interracial relationships at the time of greatest migration. Additionally, the number of Native Americans surviving European settlement living in western states was significantly higher than in the ***73** east, which helps to explain the Native-American "admixture" in African-American mtDNA profiles. [FN94]

A further critical dimension of regional variation in mtDNA profiles is a result of the variation in the level of "admixture" between African Americans and other groups around the country. For example, while African Americans living in Charleston, South Carolina, possess about 6.5% of European maternal ancestry, this figure is much higher in Baltimore (14.94%), New York (9.11%), and Pittsburgh (9.9%). [FN95] To determine the frequency of an mtDNA sequence at a Charleston crime scene, for example, a forensic scientist should use a database that takes into account the types of mtDNA profiles that exist in Charleston. As further illustration, Jamaican Americans, whose mtDNA is on average 12.93% derived from European ancestry, have quite different mtDNA profiles from African Americans in most American cities — information that should be known to the forensic scientist in electing to which mtDNA database to compare the questioned profile. [FN96] The SWGDAM database does not account for, or reflect, these regional differences.

4. Population Substructure with Respect to MtDNA Sequences in the United States and Other, Non-African-American Ancestral Populations

The SWGDAM database also fails to account for regional variation in other U.S. ethnic groups. For example, while the database has a Hispanic category, most geneticists agree that the term "Hispanic" is primarily a language-based categorization, not a genetic one. [FN97] Not surprisingly, then, individuals in the linguistic category "Hispanic" display tremendous amounts of genetic variation. [FN98] One cannot reasonably claim, for example, that Hispanics living in South Florida (largely of Cuban and Puerto Rican ancestry) are genetically representative of Hispanics living in California (largely Mexican in ancestry). Yet the design of the SWGDAM mtDNA database assumes that mtDNA profiles of Hispanic-*74 Americans are randomly distributed. This failure to account for genetic diversity is particularly troubling given that the FBI *does* distinguish between Southeast and Southwest Hispanics in its *nuclear* DNA database, presumably to account for population substructure within the "Hispanic" population. [FN99] The FBI's attempt to subcategorize its (more recombinant) nDNA database to account for substructure is laudable, but the lack of recombination in mtDNA inheritance makes geographic clustering all the more critical in designing a representative mtDNA population database.

A simple contrast between the SWGDAM database and various compilations of mtDNA sequences observed in the published literature highlights the database's lack of geographic representation. For example, the SWGDAM database contains only two categories of Native-American mtDNA profiles, Apache and Navajo, which contain 180 and 146 mtDNA sequences, respectively. These SWGDAM sub-databases are incomplete and unrepresentative. Haplogroup D exists in Apache anthropological databases but is completely missing from the SWGDAM Apache database. [FN100]

The frequency of Haplogroup X in studies in the academic literature is four-to-five times greater than in the corresponding SWGDAM database. [FN101] More generally, the collections of mtDNA sequences in the research literature — which are approximately one-third the size of the SWGDAM database — report entire haplogroups not present in the SWGDAM database and significantly different percentages of the kinds of haplotypes represented in the SWGDAM database. [FN102]

The same issue of disproportionate representation of sub-populations is also reflected in SWGDAM's East Asian databases. The database fails to account for the proportional ancestry of East Asian Americans. The 753 individuals in the SWGDAM East Asian database are from China, Korea, Japan and Thailand, with almost half from China. [FN103] Significant disconnect exists between the SWGDAM *75 database and the 2000 U.S. Census figures. [FN104] For example, based on the 2000 Census, 18.3% of the U.S. Asian population is Filipino, while there are no Filipinos in the SWGDAM database. [FN105] Similarly, the percentage of Chinese and Korean individuals in the SWGDAM database is double that reflected in the Census, while the database's percentage of Asian-Indians is one-seventh of their true percentage of the population in 2000. Simply put, the SWGDAM database is not representative of the distribution of Asian-American source populations. [FN106]

The Caucasian database is also problematic in its apparent failure to account for non-random distribution of ancestral haplogroups. Those who argue that SWGDAM's Caucasian database is representative point to the fact that its samples include 44.2% of the H Haplogroup, which appears in approximately the same proportion in certain Western European countries. [FN107] But the percentage of "H" varies widely outside a handful of countries in Western Europe, such as countries in Scandinavia, Eastern Europe, and parts of West Europe such as France, Northern Germany, and Scotland — areas where, of course, many American *76 families originated. [FN108]

In sum, the SWGDAM database appears to misrepresent the regional genetic diversity of mtDNA profiles to ignore studies showing tremendous intra-group diversity in the various macro-ethnic categories represented in the database. The database combines internally heterogeneous groups under broad rubrics without a demonstration that the deviation from homogeneity would have negligible consequences in reporting mtDNA match significance. If the database is not representative, it does not serve its intended purpose of providing a random selection of the relevant population from which re-

liable sequence frequency estimates may be calculated. In turn, if the database does not produce reliable frequency estimates, its admissibility under the prevailing rules for admission of scientific evidence would, as discussed below in Part IV, seem to be questionable at best. [FN109]

B. The Size of the SWGDAM Database

Given the degree of known mtDNA genetic variation, the SWGDAM database, whether the surveyed category contains 8 profiles (the Pakistani category of the database), 1148 profiles (the African-American category of the database), or 5071 profiles (the total number of profiles in the database), is too small to provide meaningful estimates of sequence frequencies. Extrapolation from small sample sizes inhibits the ability to make meaningful mtDNA profile frequency estimates, and statistical claims about frequency estimates based on databases smaller than one hundred profiles are particularly questionable. [FN110] While the larger categories such as the Caucasian, African-American, and Hispanic databases may appear to contain a considerable number of profiles, such appearances are misleading. Even the relatively larger databases are insufficient, both because the validation work ***77** underlying those databases is incomplete [FN111] and because individuals in those categories come from a much wider geographic range than the smaller, more narrowly targeted databases.

Take the African-American database, containing 1148 profiles, as an example. Assume, for the sake of illustration, that the database contains 1200 profiles and is representative of the relevant population. Given that many mtDNA profiles occur with a frequency of at least 1 per 1000, or 0.1%, one can state that there is a 99.9% chance that any particular person in the relevant population will *not* exhibit this profile. In a 1200-sequence database presumed to be representative, the probability of completely missing a profile that is as common as 1 in 1000 is 30.1%. [FN112] In an *unrepresentative* database, where the distribution of sequence frequencies is unknown, such a probability cannot even be calculated. To predict the frequency of a given mtDNA frequency, the database needs to be both representative *and* sufficiently large.

Any determination of how large the database must be to provide accurate frequency estimates must take into account what scientists presently know about mtDNA haplotype frequencies. For example, over 50% of known mtDNA sequences have been observed just one time. [FN113] Therefore, in a database of one thousand samples, one would expect that five hundred of the samples occur only once in the database. If an additional 1000 individuals were sampled, the likelihood that those same five hundred samples would each be observed only once decreases significantly. In addition, given that mtDNA sequence frequencies in the population are yet unknown, ancestral categories not yet accounted for in the SWGDAM database may have significantly higher or lower frequencies of unique sequences. So as not to underestimate the frequency of a suspect's profile in determining the probative value of a "match," databases should be constructed to ***78** minimize the probability of missing a rare profile and to maximize the probability that the database represents all possible profiles in the relevant population.

To the authors' knowledge, no published article on mtDNA typing has suggested how large a database would have to be to generate accurate mtDNA sequence frequency statistics for forensic use, and the authors do not speculate in this article as to how large such a forensic database would have to be. Scientists are still in the process of collecting mtDNA samples and determining the extent of geographic and ancestry-related substructure in the distribution of mtDNA profiles. The scientific community must arrive at an accurate estimate of the level of mtDNA variation, and the distribution of profiles, in the population before determining how many, and what type of, samples would be necessary to create a statistically sound forensic mtDNA database.

C. Quality Control Issues

There is reason to believe that the SWGDAM database contains errors that potentially affect the quality of the data and therefore potentially undercut the ability of the database to generate accurate statistical estimates. Not surprisingly, mtDNA sequencing — which involves typing the 600-base HVI/II region and hand-transcribing the positions at which the sequence differs from the CRS — results in many more transcription errors than does nDNA testing. [FN114] Human errors also stem from incorrect recording or exchanging of laboratory samples or misreading of machine outputs. [FN115] Outside scientists have found several transcription errors in the SWGDAM database. [FN116] Upon the publishing of such errors, the FBI has conducted its own studies and found even more errors. [FN117]

The lack of quality control has subjected the SWGDAM database to international**79** criticism. For example, several European scholars, after inspecting the database for errors, have written about its "poor quality," saying that reliance on its utility "inhibit[s] the generation of a new reliable mtDNA database in the United States." [FN118]

For the African-American database, the researchers conducted a phylogenetic analysis — the use of computer algorithms to detect inconsistencies in the evolutionary position of individual sequences resulting from miscoding or recombining of computer records during data entry — and observed "a number of major deficiencies," suggesting a confusion of specimens in the laboratory or faulty data entry. [FN119] Because the FBI's raw data is not publicly available for reexamination and correction by independent scientists, the European scientists were unable to manually look for errors; instead, the FBI was notified of their findings with the hope that the FBI would conduct a comprehensive investigation into the accuracy of the database profiles. [FN120]

Instead, the FBI's response to these reports of errors was to conduct only a partial inquiry for error correction. [FN121] Specifically, when notified of the findings of error by the European scholars, the FBI conducted a phylogenetic analysis and partial manual verification of its database, uncovering additional errors. Despite finding a number of errors in the manual verification process, the FBI only checked a small percentage of the SWGDAM profiles manually. For example, only 196 of the 1148 sequences in the African-American database were so checked, [FN122] leaving unknown how many other errors exist in the African-American database or in the other subpopulation databases. Given that only the FBI has the ability to conduct a complete inquiry into errors in its database, and that the FBI currently refuses to grant non-employees uncontrolled access to its raw data, [FN123] no apparent means exist for independent reviewers to ensure that the SWGDAM database is now free of such errors. [FN124]

*80 *D. Problems with the Counting Method*

The present method of estimating the frequency of a sequence in the population — counting the number of hits in the SWGDAM forensic database and calculating an upper-bound confidence interval around that number — does not take into account the observations of the profile in the suspect sample and in the evidence sample. In cases in which the suspect sample and the evidence sample are consistent for reasons other than the suspect being the source, this approach systematically underestimates the frequency of questioned mtDNA profile in the relevant population. This issue should be addressed and resolved by attorneys and courts, given the effect such underestimations can have on the presumption of innocence.

Again, consider the hypothetical in which a suspect's mtDNA sequence is consistent with that found at the crime scene, and the shared profile is compared to the SWGDAM African-American database, where the number of profiles is 1148 (n = 1148) and where the database is assumed to be representative and random. If an examiner searches the database and does not find the shared profile, she reports the number of hits as zero, reporting that the suspect's profile has never been seen before in the database. But the suspect's profile has arguably been seen twice: once in the suspect himself and once in the evidence sample. Failing to count the observation of the profile in the suspect as a hit in the database

seems to ignore useful and relevant information. The suspect is, after all, part of the relevant population, and there appears to be no reason to consider him outside the scope of the database of profiles. Thus, rather than conduct a frequency estimate based upon zero hits in a database of 1148 samples, the examiner should, at the very least, conduct a frequency estimate based upon one hit in a database of 1149 (n+1) samples.

Moreover, the election to disregard the observation of the profile in the suspect's sample and in the evidence sample may implicate the presumption of innocence. Most jurisdictions have a jury instruction providing that, unless and until the suspect is proven guilty by the prosecution and the jury renders a verdict of guilty, the suspect in a criminal trial is presumed innocent in the eyes of the jury. [FN125] If that ***81** presumption is taken seriously, the evidence sample and the suspect's sample should not be presumed to confirm the same person. After all, the question of whether or not the suspect actually contributed the sample is the very question to which the mtDNA frequency estimate is relevant. Thus, the most appropriate assumption is that the suspect's profile has been seen twice: once in the evidence sample and once in the suspect's sample. Therefore, in the hypothetical, the FBI should conduct a frequency estimate based upon two hits in a sample of 1150 (n+2) sequences. [FN126] Such modifications to the "counting method" affect — in some cases, dramatically so [FN127] — the reported frequency estimates and therefore should be provided to the jury.

IV. COMMUNICATION OF SWGDAM DATABASE ISSUES TO COURTS AND JURIES THROUGH ADMISSIBILITY CHALLENGES

Notwithstanding these inherent problems with using the SWGDAM database to calculate the statistical significance of a mtDNA "inclusion," the burgeoning use of mtDNA evidence in criminal trials throughout the country has continued unabated. The reason, as discussed below, is not that large numbers of courts have rejected challenges based on these problems; rather, courts and defense counsel are generally not *aware* of the existence or scope of the scientific dispute over the reliability of the FBI's methods. It is critical that courts be apprised of these issues through admissibility challenges so that they may have the opportunity to examine the issues and ensure that only reliable scientific evidence is used against criminal ***82** defendants.

A. *Legal Standards Governing Admission of Scientific Evidence*

Most U.S. courts employ one of two tests to determine admissibility of novel scientific evidence. A number of jurisdictions follow *Frye v. United States*, [FN128] admitting novel scientific evidence only when the methodology used is "generally accepted" in the relevant scientific community. [FN129] Still others, including the federal courts, follow the test set forth by the Supreme Court in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, [FN130] in which the Court construed the Federal Rule of Evidence governing admission of expert testimony to require that trial judges make an independent judicial determination whether the scientific evidence is sufficiently reliable. [FN131] Still other courts follow some combination of the two dominant approaches or another, more idiosyncratic approach. [FN132] Because the vast majority of jurisdictions subscribe to either *Frye*, *Daubert*, or a hybrid standard, this section focuses on the two dominant standards.

The *Frye* standard requires that the scientific community approve of a technique before it may be used in courts. If scientists, significant either in number or expertise, publicly oppose a new technique as unreliable, the trial judge must exclude the evidence. [FN133] The *Frye* standard is inherently conservative in that it requires those experts who are in a position best to understand and review a procedure to pass on its reliability. While the waiting period that scientific evidence and techniques must endure before gaining legal acceptance under *Frye* ***83** has generated criticism, [FN134] the *Frye* standard remains the standard for admission of scientific evidence in a number of jurisdictions.

In *Daubert*, the Supreme Court rejected the *Frye* standard for use in federal court and concluded that that the Federal Rules of Evidence require judges to act as gatekeepers, making a "preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts at issue." [FN135] The Supreme Court set out a flexible and nonexclusive list of factors for courts to consider, including (1) whether the science underlying the questioned evidence can be, and has been, empirically tested; (2) whether the science has been subjected to peer review and publication; (3) whether there is a known or potential rate of error; (4) whether standards exist and are maintained to control the technique's operation; and (5) whether the scientific proposition at issue has been generally accepted. [FN136] If, after considering these and any other relevant factors, the trial judge determines that the scientific methodology is both "reliable" and "fit[s]" the circumstances of the case, [FN137] the evidence is admissible. [FN138] While *Daubert* involved interpretation of a Federal Rule, many states have adopted the *Daubert* standard. [FN139]

As numerous commentators have observed and courts have held, evidence of a DNA inclusion or match has little meaning without a sense of the frequency of the profile in the population. [FN140] If the frequency of a profile from evidence at the crime scene were found in 99% of the general population, for example, the fact that the defendant is a potential contributor would have only nominal probative value. And while expert testimony as to frequency statistics may not be necessary where the issue is the frequency of people with blond hair or other information easily accessible through common human experience, most jurors have little if any ***84** intuition as to the relative frequencies of mtDNA sequences in the population. [FN141] Thus, as a legal matter, the statistical methodology used to estimate the significance of an inclusion or match must independently pass muster under either the *Frye* or *Daubert* standard of admissibility for scientific evidence.

Neither *Daubert* nor *Frye* sets a more "lenient" threshold for admissibility than the other; both require a pretrial showing of scientific validity. The principal distinction between the two lies in the question, "who decides the issue of scientific validity?" Under *Frye*, the trial court defers to the opinions of scientists as to whether a particular scientific advancement is valid. Under *Daubert*, the court considers the views of scientists but, ultimately, the court itself determines the scientific validity of the evidence. Under either standard, evidence with a strong scientific foundation will likely be admitted; evidence lacking such a foundation will likely be excluded. [FN142] For the reasons given in Part III, this Article submits that forensic mtDNA does not yet have a strong enough scientific underpinning to satisfy either the *Frye* or *Daubert* standards for admissibility, and courts should take great care prior to admitting such evidence — whether by the prosecution seeking to inculpate a defendant or by the defense seeking to convince the jury that an uncharged third party is the true perpetrator.

B. *The Importance of Well-Litigated Admissibility Challenges to the Reliability of MtDNA Evidence Used Against Criminal Defendants*

The stakes in admitting mtDNA evidence without a proper scientific foundation are high; because reliance on the SWGDAM database potentially underestimates the frequency statistic, jurors typically hear that the defendant belongs to the less than 1% of the population who could have contributed the mtDNA, and, therefore, are given the sense that the defendant likely committed the offense. [FN143] An additional concern is that jurors will confuse mtDNA with nDNA, which has an ***85** aura of infallibility from its coverage in the popular press and is viewed as having an almost mysterious quality as a tool of identification. In fact, recent jury studies suggest that jurors may confuse different types of DNA, and may see all DNA evidence as infallible. [FN144]

If litigants do not timely apprise trial judges of these scientific issues, courts will not have the opportunity to determ-

ine whether, in light of such issues, the proffered mtDNA inclusion statistics that will be reported to the jury are scientifically unsound or are not generally accepted in the scientific community. Due in large part to the fact that mtDNA evidence is often admitted against a defendant without any challenge to its admissibility, most courts are simply unaware of the unique aspects of mtDNA typing as compared to nDNA typing, and have not been exposed to the scientific literature discussing the problems with the SWGDAM database. While the majority of the few courts that *have* ruled on the admissibility of mtDNA evidence have approved of its use against a defendant, judicial consideration of this form of evidence is in its infancy. To date, only two published opinions from federal courts address the admissibility of mtDNA evidence, along with a handful of published state trial and appellate decisions. Significantly, no state court of last resort has yet ruled mtDNA evidence admissible under a *Frye*-type standard. [FN145] Only one federal appellate court and two state supreme ***86** courts have ruled mtDNA admissible under a *Daubert*-like standard. [FN146] In many of these cases, the evidence was admitted without the trial court ever hearing a witness contrary to the government's forensic scientist vouching for admission of the evidence. [FN147] None of the published decisions discusses in a meaningful way problems with the content of the databases used to generate frequency statistics. [FN148] In addition, scholars in legal academia, while recognizing general issues with respect to admission of mtDNA evidence in criminal trials, have not yet begun to discuss the database problems at length. [FN149]

The lack of awareness on the part of courts and other participants in the legal system with respect to the problems with the SWGDAM database and other important scientific issues is compounded by the fact that most practicing forensic scientists are not part of, and perhaps not even aware of, the conversation taking place among medical geneticists, evolutionary biologists, and molecular anthropologists concerning the extent of genetic individuality and diversity of mtDNA. [FN150] Additionally, because most criminal defendants do not have the resources to mount complicated, expensive admissibility challenges to forensic mtDNA evidence, the ***87** emerging and accumulated knowledge of scientists who regularly work outside the legal system appears not to be making its way into courtrooms before judges and juries. Professors Mildred Cho and Pamela Sankler express the need to bridge the gap between science inside, and outside, the courtroom:

> [The] series of arguments and counterarguments about the association between 'race' and patterns of DNA markers [that] has been unfolding in the medical genetics literature over the last four years ... are relevant to, and should include, forensic geneticists.... These conversations are directly relevant to the forensics genetics community[, but they] have not been widely extended into this group. There is an urgent need to expand this debate into the field of forensics. [FN151]

While hiring experts to testify at admissibility hearings may be beyond a particular defendant's means, individual attorneys and defender institutions should at the very least bring to courts' attention the scientific studies discussed in articles such as this one, so that courts will begin to take notice of evidence of both a lack of general acceptance in the scientific community of using the SWGDAM database to generate mtDNA frequency estimates, which may render the mtDNA evidence inadmissible under *Frye*, and a lack of scientific validity in using the database, evidence that, if accepted, would potentially render the mtDNA evidence inadmissible under a *Daubert*-like standard.

CONCLUSION

What can be done to ensure that mtDNA evidence is used fairly and effectively as "inclusion" evidence? In the first instance, both forensic scientists and the broader scientific community should work to improve the science of mtDNA frequency statistics to provide a sufficient scientific underpinning for mtDNA to support its admission in criminal cases. Scientists should also follow the lead of laboratories such as AFDIL by increasing the discriminatory power of mtDNA typing and decrease the chance of a false inclusion, by typing additional locations in both the control region and coding

region of the mtDNA genome, and by taking advantage of SNP technology.

Additionally, the SWGDAM forensic mtDNA database should be corrected and expanded. Specifically, before mtDNA evidence is used as inclusion evidence in the courtroom, the scientific community should collect more data on human migration patterns, including migration patterns within the United States, to identify possible locations of mtDNA clusters based on historical developments. Upon generating that data, the scientists should conduct phylogeographic as well as phylogenetic studies to determine not only the full diversity of mtDNA **88** sequences in the population, but the geographic distribution of such sequences as well. Upon understanding the geographic distribution of such sequences, the criminal justice community should develop *regional* databases that reflect uneven geographic distribution of mtDNA sequences. In doing so, efforts should be made to vastly increase the number of sequences in those databases over the current size, by additional sampling and by accessing the raw data from the published academic studies and adding that data to the regional forensic databases.

Furthermore, because databases are only useful if their data are accurate, forensic scientists should develop and implement an additional quality assurance procedure to create a systematic means of identifying, minimizing, and correcting database errors, including the implementation of quality control measures urged by AFDIL and other reputable laboratories. Forensic scientists should also open up the raw data of the sequences in the SWGDAM database to independent researchers to permit outside review of the database, and immediately implement a complete manual verification of every sequence in the database, double-checked visually and by hand, base-pair by base-pair. Errors should not be accepted.

Moreover, we suggest modification in the counting method, by accounting for the observation of the profile in the suspect and the evidence sample when determining the number of "hits" in the database, and using a 99% confidence interval to reflect the grave need to avoid error in criminal trials. Such a process accords more with a constitutional presumption of innocence.

Finally, prosecutors, defense attorneys, and judges must be vigilant in ensuring the reliability of mtDNA evidence admitted in criminal trials. As Professor Michael Saks notes, the true "'revolution' of *Daubert* lies" in the fact that "[j]udges and lawyers, long insulated from the scientific revolution, are now obligated to become familiar with the methods and culture of science." [FN152] As scientists and legal professionals work to foster an understanding of the "methods and culture of science" in the courtroom, genuinely reliable evidence will appear before juries, promoting greater confidence in the outcome of criminal trials.

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[FN1]. The first use of nuclear DNA in a criminal trial was in a Florida sexual assault trial in 1987. *See* NORAH RUDIN & KEITH INMAN, AN INTRODUCTION TO FORENSIC DNA EVIDENCE 186, 187 (2d ed. 2001) (discussing *Florida v. Andrews*).

[FN2]. *See, e.g.*, Max M. Houck & Bruce Budowle, *Correlation of Microscopic and Mitochondrial DNA Hair Comparisons*, 47 J. FORENSIC SCI. 1, 4 (2002) (noting that mtDNA has been used to exclude suspects who were originally included falsely based on microscopic hair analysis).

[FN3]. The term "match" in the context of forensic mtDNA typing is misleading because mtDNA is maternally inherited and nonrecombinant and therefore is not a unique identifier. *See* discussion *infra* at 58-99.

[FN4]. *See, e.g.*, DAVID L. FAIGMAN ET AL., 3 MODERN SCIENTIFIC EVIDENCE § 25-1.2.1 (2d ed. 2002) (listing criminal cases admitting mtDNA evidence against defendant). The federal government is in the process of greatly expanding its use of mtDNA typing in criminal cases. *See The FBI Selects 4 Regional MtDNA Laboratories*, 6 FORENSIC SCI. COMM. (Jan. 2004), *available at* http://www.fbi.gov/hq/lab/fsc/backissu/jan2004/shortcomm/2004_01_short02.htm ("As laboratories become operational during the next two years, the effect will be to double the FBI's capacity to deliver no-cost mtDNA analysis to the criminal justice system.").

[FN5]. *See, e.g.*, United States v. Porter, 618 A.2d 629, 640 (D.C. 1992) ("[I]t is the probability feature which is at the very core of the DNA evidence."); United States v. Cuff, 37 F. Supp. 2d 279, 282 (S.D.N.Y. 1999) (same). *See generally* David H. Kaye & George F. Sensabaugh Jr., *Reference Guide on DNA Evidence, in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 545 (2d ed. 2000) (citing cases for proposition that "many courts have held that a DNA match is inadmissible unless the expert attaches a scientifically valid number to the figure"); NATIONAL RESEARCH COUNCIL, THE EVALUATION OF FORENSIC DNA EVIDENCE 192 (1996) (discussing the statistical basis for interpretation) [hereinafter NRC II (1996)]; NATIONAL RESEARCH COUNCIL, DNA TECHNOLOGY IN FORENSIC SCIENCE 74-75 (1992) (discussing the meaning of "match") [hereinafter NRC I (1992)].

[FN6]. *See Bylaws of the Scientific Working Group on DNA Analysis Methods*, 5 FORENSIC SCI. COMM. (Apr. 2003), *available at* http:// www.fbi.gov/hq/lab/fsc/backissu/april2003/swgdambylaws.htm (noting that FBI Director charged SWGDAM with reviewing DNA laboratory protocols, sets terms of SWGDAM members, receives SWGDAM recommendations, and provides SWGDAM with resources, including staff, travel and lodging budget). The version of the SWGDAM database currently used in forensic testing was made public in 1999. *See* Mark R. Wilson et al., *Further Discussion of the Consistent Treatment of Length Variants in the Human Mitochondrial DNA Control Region*, 4 FORENSIC SCI. COMM. (Oct. 2002), *available at* http:// www.fbi.gov/hq/lab/fsc/backissu/oct2002/wilson.htm.

[FN7]. While the SWGDAM database classifies individuals by "race," we believe that the more accurate classification for mtDNA profiles is by ancestry and use that terminology in discussing classifications in genetic lineages.

[FN8]. *See* Keith L. Monson et al., *The MtDNA Population Database: An Integrated Software and Database Resource for Forensic Comparison*, 4 FORENSIC SCI. COMM. (Apr. 2002), *available at* http:// www.fbi.gov/hq/lab/fsc/backissu/april2002/miller1.htm (explaining database comparison method); FBI Laboratory DNA Unit II, Mitochondrial DNA Sequencing Protocol § 11.4.1 (2004) [hereinafter FBI MtDNA Protocols (2004)] (explaining counting method used by FBI when comparing profile to database).

[FN9]. *See* discussion *infra* at 76-78.

[FN10]. Because the prosecution bases its frequency estimate solely on the number of "hits" in the database, the number reported to the jury in *any* case involving a mtDNA sequence not observed in the SWGDAM database, regardless of the geographical origin, ancestry, or other characteristic of the suspect, will be identical. *See* FBI MtDNA Protocols, *supra* note 8, at § 11.4.4 (stating FBI reports 95% confidence interval around number of "hits" in every case, without consideration of other variables, such as ancestry or geographical origin).

[FN11]. Base pairs consist of pairs of nucleotides that are bound to each other across the double helix of DNA (Adenine pairing with Thymine, Guanine pairing with Cytosine). The order of the base pairs encodes the genetic instructions.

[FN12]. *See* JOHN M. BUTLER, FORENSIC DNA TYPING, 242 (2d ed. 2005).

[FN13]. *Human Mitochondrial DNA — Amplification and Sequencing Standard Reference Materials* 1-2, NAT'L INST. OF STANDARDS AND TECH SPEC. PUB. NO. 260-155 (Sept. 2003).

[FN14]. *See* Stephen Anderson et al., *Sequence and Organization of the Human Mitochondrial Genome*, 290 NATURE 457, 457-65 (1981); Mitchell M. Holland & Thomas J. Parsons, *Mitochondrial DNA Sequence Analysis: Validation and Use for Forensic Casework*, 11 FORENSIC SCI. REV. 21, 24 (Feb. 1999).

[FN15]. Anderson et al., *supra* note 14, at 457; Thomas Parsons & Michael Coble, *Increasing the Forensic Discrimination of Mitochondrial DNA Testing Through Analysis of the Entire Mitochondrial DNA Genome*, 42 CROATIAN MED. J. 304, 304 (2001).

[FN16]. *See, e.g.*, Bruce Budowle et al., *Genotype Profiles for Six Population Groups at the 13 CODIS Short Tandem Repeat Core Loci and Other PCR-Based Loci*, 1 FORENSIC SCI. COMM. (July 1999), *available at* http://www.fbi.gov/hq/lab/fsc/backissu/july1999/budowle.htm.

[FN17]. Holland & Parsons, *supra* note 14, at 24.

[FN18]. Anderson et al., *supra* note 14, at 457; Richard M. Andrews et al., *Reanalysis and Revision of the Cambridge Reference Sequence for Human Mitochondrial DNA*, 23 NATURE GENETICS 147 (Oct. 1999).

[FN19]. *See, e.g.*, Carla Bini & Stefania Ceccardi et al., *Different Informativeness of Three Hypervariable Mitochondrial DNA Regions in the Population of Bologna (Italy)*, 135 FORENSIC SCI. INT'L 48 (2003); Sabine Lutz & Holger Wittig et al., *Is It Possible to Differentiate MtDNA By Means of HVIII In Samples That Cannot Be Distinguished By Sequencing the HVI and HVII Regions?*, 113 FORENSIC SCI. INT'L 97 (2000).

[FN20]. Lutz & Wittig, *supra* note 19, at 97.

[FN21]. *See* Michael D. Coble et al., *Single Nucleotide Polymorphisms Over the Entire MtDNA Genome that Increase the Power of Forensic Testing in Caucasians*, 118 INT'L J. LEGAL MED. 137, 143-44 (2004) (discussing typing of SNPs, including position 16519, which is outside of HVI and HVII and has greatest variability in entire mtDNA genome); Luisa Pereira et al., *Evaluating the Forensic Informativeness of MtDNA Haplogroup H Sub-Typing on a Eurasian Scale*, FORENSIC SCI. INT'L, *available at* http://www.sciencedirect.com (2005) (discriminating otherwise identical haplotypes by sequencing eight coding region SNPs); Yong-Gang Yao et al., *Phylogeographic Differentiation of Mitochondrial DNA in Han Chinese*, 70 AM. J. HUM. GENETICS 635, 648 (2002) (noting that "[c]oding region information is indispensable for phylogenetic analysis of mtDNA").

[FN22]. *See* Coble et al., *supra* note 21, at 143-44 (discussing how further typing of regions outside HVI and HVII would

require development of new databases and other costly and laborious efforts).

[FN23]. Parsons & Coble, *supra* note 15, at 305. *See also* Coble et al., *supra* note 21, at 137 (discussing the study about sequencing entire mtDNA genome to increase forensic discrimination); Rebecca S. Just et al., *Toward Increased Utility of MtDNA in Forensic Identifications*, 146S FORENSIC SCI. INT'L S147 (2004) (discussing preliminary results of large-scale databasing project targeting populations underrepresented in current forensic mtDNA databases); Thomas J. Parsons et al., Report for U.S. Dep't of Justice, Office of Justice Programs, Progress of Project 2000-IJ-CX-K010, Homogeneous Fluorescent PCR Assays over the MtDNA Genome, up to June 30, 2005, provided in response to OJP FOIA No. 05-00258 (on file with authors) (explaining that, from 2000 to 2005, AFDIL has sequenced hundreds of full mtDNA genomes in the African-American, Hispanic, and Central Asian populations in an effort to better account for documented regional variation in mtDNA sequence frequencies).

[FN24]. BUTLER, *supra* note 12, at 20.

[FN25]. *See* D. Andrew Merriweather & Frederika A. Kaestle, *Mitochondrial Recombination? (Continued)*, 285 SCI. 835 (1999) (concluding mtDNA is maternally inherited and finding no evidence for mtDNA recombination in humans). Other scientists have reported observations of "recombination" — mixing between maternal and paternal mtDNA in offspring. *See* Adam Eyre-Walker, Noel Smith & John Maynard Smith, *How Clonal Are Human Mitochondria?*, 266 PROC.: BIOLOGICAL SCI. 477 (1999). These observations are disputed. *See, e.g*., Joanna L. Elson et al., *Analysis of European MtDNAs for Recombination*, 68 AM. J. HUM. GENETICS 145, 145 (2001) (disagreeing with Eyre-Walker results and concluding "that there is no compelling reason to overturn the standard paradigm of clonal mtDNA transmission in humans"); Peter Forster, *To Err Is Human*, 67 ANNALS OF HUM. GENETICS 2 (2003) (same). There have been some observations of paternal inheritance, *see* Marianne Schwartz & John Vissing, *Paternal Inheritance of Mitochondrial DNA*, 347 NEW ENGLAND J. OF MED. 576, 579 (Aug. 22, 2002) (observing paternal inheritance of pathogenic mtDNA), but the phenomenon of paternal inheritance is an exception, if not a well understood one, to the general rule of maternal inheritance.

[FN26]. Bruce Budowle et al., *Forensics and Mitochondrial DNA: Applications, Debates, and Foundations*, 4 ANN. REV. GENOMICS & HUM. GENETICS 119, 121 (2003).

[FN27]. *See id*. at 128 ("A decade ago, most individuals were thought to be homoplasmic."); Terry Melton, *Mitochondrial DNA Heteroplasmy*, 16 FORENSIC SCI. REV. 1, 3 (Jan. 2004).

[FN28]. Walter Bär et al., *Guidelines for Mitochondrial DNA Typing*, 79 VOX SANGUINIS 121, 122 (2000) ("[I]t is now thought that all individuals are heteroplasmic at some level."); Melton, *supra* note 27, at 2 ("[I]t is also certain that some degree of heteroplasmy exists in all individuals.").

[FN29]. *See* John Buckleton, Simon Walsh, & Sallyann Harbison, *Nonautosomal Forensic Markers, in* JOHN BUCKLETON, CHRISTOPHER M. TRIGGS & SIMON J. WALSH, EDS., FORENSIC DNA EVIDENCE INTERPRETATION 303 (2005) (discussing various theories); Peter D'Eustachio, *High Levels of Mitochondrial DNA Heteroplasmy in Human Hairs by Budowle et al*., 130 FORENSIC SCI. INT'L 63, 63 (2002) ("Major unresolved issues include the molecular mechanisms responsible for the occurrence of heteroplasmy to different extents in different tissues, and the possibility that heteroplasmy levels in an individual might vary with age.").

[FN30]. Buckleton et al., *supra* note 29, at 304 (stating routine-sequencing methods cannot detect heteroplasmy above sequencing background noise unless it approaches 20%).

[FN31]. Mark R. Wilson et al., *A Family Exhibiting Heteroplasmy in the Human Mitochondrial DNA Control Region Reveals Both Somatic Mosaicism and Pronounced Segregation of Mitotypes*, 100 HUM. GENETICS 167, 167 (1997).

[FN32]. The NRC's 1992 and 1996 reports on forensic DNA typing both contain lengthy discussions of population substructure in the database used by the FBI to generate nDNA frequency tables and, using the product rule, a "random match probability" over the thirteen locations used in forensic nDNA testing. NRC II (1996), *supra* note 5, at 122-23; NRC I (1992), *supra* note 5, at 74-77.

[FN33]. *See* discussion *infra* at III.

[FN34]. Marc W. Allard et al., *Characterization of the Caucasian Haplogroups Present in the SWGDAM Forensic MtDNA Dataset for 1771 Human Control Region Sequence*, 47 J. FORENSIC SCI. 1215, 1219 (2002).

[FN35]. *Id*. *See also* Sarah A. Tishkoff et al., *Genetic Analysis of African Populations: Human Evolution and Complex Disease*, 3 NATURE REVIEWS - GENETICS 611 (2002).

[FN36]. *See, e.g.*, Douglas C. Wallace, *Mitochondrial Disease in Man and Mouse*, 283 SCI. 1482, 1482 (1999).

[FN37]. *See, e.g.*, Mark Shriver & Rick Kittles, *Genetic Ancestry and the Search for Personalized Genetic Histories*, 5 NATURE REVIEWS - GENETICS 611, 611 (2004); Anne C. Stone, James E. Starrs, & Mark Stoneking, *Mitochondrial DNA Analysis of the Presumptive Remains of Jesse James*, 46 J. FORENSIC SCI. 173, 173 (2001) (using mtDNA to determine if particular remains could be those of Jesse James); Lev A. Zhivotovsky, *Recognition of the Remains of Tsar Nicolas II and His Family: A Case of Premature Identification?*, 26 ANNALS HUM. BIOLOGY 569, 569 (1999).

[FN38]. *See, e.g.*, Rebecca L. Cann et al., *Mitochondrial DNA and Human Evolution*, 325 NATURE 31, 31 (1987); Frederika A. Kaestle & K. Ann Horsburgh, *Ancient DNA in Anthropology: Methods, Applications, and Ethics*, 45 YEARBOOK OF PHYS. ANTHROP. 92 (2002); Frederika A. Kaestle & David Glen Smith, *Ancient Mitochondrial DNA Evidence for Prehistoric Population Movement: The Numic Expansion*, 115 AM. J. PHYS. ANTHROP. 1-12 (2001) (using ancient and modern mtDNA to test hypothesis that modern Native American inhabitants of Nevada are recent arrivals who replaced previous inhabitants); Ripan S. Malhi et al., *Patterns of MtDNA Diversity in Northwestern North America*, 76 HUM. BIOLOGY 33, 33-34 (2004) (using ancient and modern mtDNA to show significant migration from sub arctic and Pacific coast into Columbian Plateau region); Stéphanie Plaza et al., *Insights into the Western Bantu Dispersal: MtDNA Lineage Analysis in Angola*, 115 HUM. GENETICS 439 (2004) (using mtDNA to clarify spread of Bantu populations throughout Africa and to trace movement of slaves into Brazil from Angola).

[FN39]. The Armed Forces DNA Identification Laboratory engages in such identification procedures using mtDNA testing for casualties from wartime and disasters. *See AFDIL Mitochondrial DNA (MtDNA) Section*, http://www.afip.org/Departments/oafme/dna/afdil/mito.html (last visited Jan. 20, 2006).

[FN40]. *See, e.g.*, Sarah Koenig, *DNA Identification Is a Daunting Task* (Sept. 20, 2001), http://www.baltimoresun.com/news/custom/attack/bal-te.dna20sep20,1,242800.story?coll=bal-attack-utility (discussing use of mtDNA typing to identify remains from September 11 bombings, the Oklahoma City bombings, and plane crashes); Yasser Daoudi et al., *Identification of Missing Individuals from Bosnia and Herzegovina Using Mitochondrial DNA Analysis*, presented at 11th International Symposium on Human Identification (2000), http://www.promega.com/geneticidproc/ussymp11proc/abstracts/daoudi.pdf. *See generally* http://www.dna.gov/uses/m_person (discussing the President's DNA Initiative, including use of mtDNA in identifying missing persons from natural disasters and crimes).

[FN41]. *See* Peter Neufeld, *Preventing the Execution of the Innocent: Testimony Before the House Judiciary Committee*, 29 HOFSTRA L. REV. 1155, 1161-62 (2001).

[FN42]. Alice A. Isenberg, *Forensic Mitochondrial DNA Analysis*, FBI LAW ENFORCEMENT BULLETIN 16 (August 2002), *available at* http:// www.fbi.gov/publications/leb/2002/august021eb.pdf.

[FN43]. Forensic mtDNA testing is far more specialized, expensive, and time-consuming than nDNA testing. Over one hundred laboratories in the United States are authorized to conduct forensic nuclear DNA analysis. Government forensic mtDNA laboratories include the FBI and AFDIL. Commercial forensic mtDNA laboratories include Bode Technology Group, Inc., in Springfield, Virginia; Laboratory Corporation of America, in Research Triangle Park, North Carolina; Mitotyping Technologies, LLC, in State College, Pennsylvania; Orchid Cellmark Dallas, in Dallas, Texas; Reliagene Technologies, Inc., in New Orleans, Louisiana; and Serological Research Institute, in Richmond, California.

[FN44]. Drs. Kaestle and Kittles have become familiar with forensic laboratories' procedures for analyzing and typing mtDNA sequences through their anthropological and genetic research involving mtDNA sequencing. Ms. Roth and Mr. Ungvarsky have become familiar with such procedures through trial and appellate litigation involving the United States' use of mtDNA typing conducted by the FBI and other laboratories as evidence in criminal trials.

[FN45]. FBI MtDNA Protocols (2004), *supra* note 8, at § 11.3.3.

[FN46]. While this Article focuses on the sequence comparison protocols followed by the FBI, it is worth noting that other mtDNA typing laboratories differ in their treatment of heteroplasmy when comparing the suspect's profile to the evidence sample profile. *See* Statement of Dr. M. Thomas P. Gilbert, submitted in *United States v. Chase*, D.C. Super. Ct. Crim. No. F-7330-99 (July 9, 2004) (on file with authors) (reviewing protocols for all major mtDNA testing laboratories and observing that "forensic laboratories come to no consensus as to how to interpret heteroplasmic sequences.... [T]he interpretation guidelines vary when determining what would be labeled as 'inconclusive' and what would be labeled as an 'exclusion."').

[FN47]. FBI MtDNA Protocols (2004), *supra* note 8, at § 11.3.3.

[FN48]. *Id*.

[FN49]. *Id*.

[FN50]. For convenience purposes, forensic laboratories do not search all 610 bases of the HVI and HVII regions. Rather, the sample is first compared to the revised CRS. Differences between the two are then searched against the profiles in the SWGDAM database. Alice R. Isenberg & Jodi M. Moore, *Mitochondrial DNA Analysis at the FBI Laboratory*, I FORENSIC SCI. COMM. 1 (1999), *available at* http:// www.fbi.gov/hq/lab/fsc/backissu/july1999/dnalist.htm.

[FN51]. *See* FBI MtDNA Protocols (2004), *supra* note 8, at § 12.1. The SWGDAM database has grown from 1393 sequences in 1998 to its current size of 5071. *See* Bruce Budowle et al., *Mitochondrial DNA Regions HVI and HVII Population Data*, 103 FORENSIC SCI. INT'L 23, 25 (1999) [hereinafter Budowle et al. (1999)] (1393 sequences in 1998); Isenberg & Moore, *supra* note 50, at 1 (2426 sequences in 1999); Constance Fisher & Bruce Budowle, Presentation, *Mitochondrial DNA: Today & Tomorrow*, 11th Annual Int'l Symposium on Human Identification (2000), *available at* http:// www.promega.com/geneticidproc/ussymp11proc/content/fisher.pdf (4142 sequences in 2000). The database has not grown at all since at least April 2003. *See* FBI MtDNA Protocols (2004), *supra* note 8, at § 12.1 (stating that the database as of April 14, 2003, "contain[s] 5071 individuals").

[FN52]. None of the sub-databases has more than 1814 profiles; ten have fewer than two hundred profiles; and five have fewer than one hundred profiles. The populations and the number of profiles within each are as follows:

Race	Number of Profiles
African-Americans	1148
Apaches	180
Caucasians	1814
Chinese/Taiwanese	356
Egyptians	48
Guam	87
Hispanics	759
India	19
Japanese	163
Koreans	182
Navajos	146
Pakistan	8
Sierra Leone	109
Thai	52
TOTAL	**5071**

Monson et al., *supra* note 8, at "Release Notes," *available at* http://www.fbi.gov/hq/lab/fsc/backissu/april2002/mtDNA_popDB1.2ReleaseNotes.pdf.

[FN53]. *See* Budowle et al. (1999), *supra* note 51, at 25 (explaining origins of SWGDAM database profiles).

[FN54]. *See id.* (listing geographical origins of SWGDAM profiles).

[FN55]. FBI MtDNA Protocols (2004), *supra* note 8, at § 11.1 (stating the FBI reports the number of "hits" in each racial database regardless of the suspect's putative race).

[FN56]. *See* Allard et al., *supra* note 34, at 2 (stating 72% of profiles in SWGDAM Caucasian database as of 2000 appear only once); Parsons & Coble, *supra* note 15, at 305:

> [C]omparing the 2000 database with the 1998 database shows that the number of sequences occurring once is decreasing, going from 63% in 1998 to 54% in 2000. The percentage of single occurrences will continue to decrease as more mtDNA samples are typed. However, the number of individuals who must be sequenced to reach the limit of mtDNA diversity is unknown [as] the overall distribution of mtDNA types is highly skewed toward rare types.

[FN57]. Laboratories use a slightly different statistical calculation when the sequence is not observed in the database. *See* Holland & Parsons, *supra* note 14, at 31-32.

[FN58]. A 95% confidence interval means that, if a series of such margins of error were constructed in estimating the frequency of the sequence in the population, approximately 95% of them should include the true frequency of the sequence in the population. Alternatively stated, there is approximately a 5% chance that the margin of error does not contain the true frequency of the sequence in the population. *See* ROBERT S. WITTE, STATISTICS 215 (2d ed. 1985). As the sample size grows, the confidence interval will become narrower, indicating 95% confidence in a smaller range of possible values for the frequency. *Id.* at 216. Ninety-nine percent confidence intervals are also "prevalent" in statistical calculations. *Id.* at 221. None of the forensic literature or forensic laboratory protocols reviewed by the authors discusses why a 95% confidence interval, as opposed to a more conservative interval like 99%, is used in forensic casework. Indeed, the FBI uses a 99% confidence interval when determining whether to label a nuclear DNA profile as "unique" in the population. *See* FBI Laboratory Unit I, Short Tandem Repeat Analysis Protocols § 10.6 at 10-10, 10-11 (Apr. 1, 2002).

[FN59]. *See, e.g.*, United States v. Coleman, 202 F. Supp. 2d 962, 964, 967 (E.D. Mo. 2002) (stating 99.93% of all persons excluded from contributing mtDNA sample); Lewis v. State, 889 So. 2d 623, 673 (Ala. Crim. App. 2003) (stating 99.8% of Caucasians excluded); State v. Pappas, 776 A.2d 1091, 1104 (Conn. 2001) (stating 99.75% of Caucasians excluded); Magaletti v. State, 847 So.2d 523, 587 (Fla. Dist. Ct. App. 2003) (stating 99.93% of all persons excluded).

[FN60]. *See* Budowle et al. (1999), *supra* note 51, at 25.

[FN61]. *See* BUTLER, *supra* note 12, at 502 ("Often the rarity of a calculated [nuclear] DNA profile goes beyond one in billions (10^9) or trillions (10^{12}) to numbers that are not frequently used because they are so large."); *id.* at 504, tbl.21.3 (listing values such as quadrillion (10^{15}), quintillion (10^{16}), and google (10^{100})).

[FN62]. *See* NRC II (1996), *supra* note 5, at 30 (stating STR database consists of convenience samples from "blood banks, paternity-testing laboratories, laboratory personnel, clients in genetic-counseling centers, law-enforcement officer, and people charged with crimes"); United States v. Bridgett, 120 Daily Wash. L. Rptr. 1697, 1700 n.12 (D.C. Super. Ct Aug. 11, 1992) (same).

[FN63]. Phylogeography "is a field of study concerned with the principles and processes governing the geographic distributions of genealogical lineages, especially those within and among closely related species [and] deals with historical, phylogenetic components of the spatial distributions of gene lineages. In other words, time and space are the jointly con-

sidered axes of phylogeography onto which (ideally) are mapped particular gene geneaologies of interest." JOHN C. AVISE, PHYLOGEOGRAPHY: THE HISTORY AND FORMATION OF SPECIES 3 (2000).

[FN64]. *See, e.g*., Ripan S. Malhi et al., *The Structure of Diversity Within New World Mitochondrial DNA Haplogroups: Implications for the Prehistory of North America*, 70 AM. J. HUM. GENET. 905, 906 (2002) [hereinafter Malhi et al. (2002)] ("significant geographic variation in frequency distributions across North America" existed for nearly five hundred Native American haplotypes and "haplogroup frequency distribution was correlated with geography"); Dan Mishmar et al., *Natural Selection Shaped Regional MtDNA Variation in Humans*, 100 PROC. NATL. ACAD. SCI. 171 (Jan. 7, 2003) ("extensive global population studies have shown that there are striking differences in the nature of the mtDNAs found in different geographic regions").

[FN65]. In North America, the C and D haplogroups, present in Native American populations, are widely distributed across the continent. *See* Malhi et al. (2002), *supra* note 64, at 909-11 & figs. 2, 3, 4. The H haplogroup occurs in 20% to 25% of the population in the Near East, 50% in Europe, and nearly 60% in the Basque country of Spain. *See* Martin Richards et al., *In Search of Geographical Patterns in European Mitochondrial DNA*, 71 AM. J. HUM. GENETICS 1168, 1170 (2002).

[FN66]. While *phylogenetic* analysis — reconstructing genetic relationships within a population — has been conducted on many of the SWGDAM racial sub-databases, such studies only show, at most, that a particular database accurately reflects most of the haplogroups that exist in the relevant population, e.g., that the Caucasian database contains all major haplogroups in the Caucasian population. *See* Allard et al., *supra* note 34, at 8. Such studies do not, however, take into account the *geographical distribution* of the sequences within the population, and thus cannot be cited as evidence that a database accurately reflects the frequency of a profile in a particular geographic area. Only *phylogeographic* studies — those that focus on the spectrum and area-specificity of major haplogroups and the haplotypes within them — can accurately determine true frequencies. *See* Juan C. Rando et al., *Phylogeographic Patterns of MtDNA Reflecting the Colonization of the Canary Islands*, 63 ANNALS HUM. GENETICS 413, 424 (1999).

[FN67]. *See, e.g*., Michael Bamshad et al., *Genetic Evidence on the Origins of Indian Caste Populations*, 11 GENOME RESEARCH 994 (2001) (discussing economic and caste distinction); Ranjan Dutta et al., *Patterns of Genetic Diversity at the Nine Forensically Approved STR Loci in the Indian Populations*, 74 HUM. BIOL. 33 (2002) (same); D. Andrew Merriwether et al., *Mitochondrial DNA Is an Indicator of Austronesian Influence in Island Melanesia*, 110 AM. J. PHYS. ANTHROPOL. 243 (1999) (linguistic distinctions); Pavao Rudan et al., *Anthropological Research of Hvar Islanders, Croatia — From Parish Registries to DNA Studies in 33 Years*, 28 COLLEGIUM ANTHROPOLOGICUM 321 (2004) (religious); Lev A. Zhivotvsky et al., *The Forensic DNA Implications of Genetic Differentiation Between Endogamous Communities*, 119 FORENSIC SCI. INT'L 269 (2001) (no obvious subdivision).

[FN68]. *See, e.g*., DAVID BALDING, WEIGHT-OF-EVIDENCE FOR FORENSIC DNA PROFILES 105-06 (2005):

> [M]aternally-related individuals might be expected to be tightly clustered, possibly on a fine geographical scale. Reports of F_{ST} estimates for mtDNA drawn from cosmopolitan European populations typically cite low values, reflecting the fact that this population is reasonably well-mixed, as well as the effects of high mtDNA mutation rates. However, researchers rarely are able to focus on the fine geographic scale that may be relevant in forensic work, and there are some large F_{ST} estimates at this scale.

see also Anita Brandstätter et al., *Mitochondrial DNA Control Region Sequences from Nairobi (Kenya): Inferring Phylogenetic Parameters for the Establishment of a Forensic Database*, 118 INT'L J. LEGAL MED. 294 (2004) (describing new forensic database containing sequences from Nairobi and finding that there were significant differences

in mtDNA compositions of this new database and the African-American SWGDAM database, as well as of published sequences from Sierra Leone, Mozambique, and United States); Peter Forster et al., *Continental and Subcontinental Distributions of MtDNA Control Region Types*, 116 INT'L J. LEGAL MED. 99, 99 (2002); Kaestle & Horsburgh, *supra* note 38, at 95 ("[M]itochondrial markers are also often geographically specific, and in some cases are limited in distribution to a single tribe (private polymorphisms)."); Rick A. Kittles & Shomarka O. Keita, *Interpreting African Genetic Diversity*, 16 AFRICAN ARCHEOL. REV. 87, 87 (1999); Luisa Pereira et al., *Prehistoric and Historic Traces in the MtDNA of Mozambique: Insights into the Bantu Expansions and the Slave* Trade, 65 AM. J. HUM. GENETICS 439 (2001); Rando et al., *supra* note 66, at 424; Antonio Salas et al., *The African Diaspora: Mitochondrial DNA and the Atlantic Slave Trade*, 74 AM. J. HUM. GENETICS 454 (2004); Yao et al., *supra* note 21, at 649.

[FN69]. Richards et al., *supra* note 65, at 255 (discussing J Haplogroup).

[FN70]. *Id*. at 254 (discussing J1b1 Haplogroup).

[FN71]. Rando, *supra* note 66, at 420, 424.

[FN72]. Pereira et al., *supra* note 68, at 452:

> There remain a large number of sequences from African haplogroups sampled in the Americas and Europe for which no match can be found in the current African database. This may be due in part to the fact that the main regions from where slaves were taken, such as Angola and the Slave Coast remain uncharacterized.

See also Joseph Lorenz et al., *African-American Lineage Markers: Determining the Geographic Source of MtDNA and Y Chromosomes* (Apr. 15, 2004), http:// www.physanth.org/annmeet/aapa2004/ajpa2004.pdf (discussing study suggesting that there is large proportion of unexamined, undocumented mtDNA variability among individuals indigenous to sub-Saharan Africa).

[FN73]. Parsons, *supra* note 23, at 1.

[FN74]. Parsons et al., *supra* note 23, at 4-5 ("U.S. Hispanics are a complex admixture of Native American, European, and African lineages, making the regional variation of U.S. Hispanics important in a forensic context."); *id*. (listing dramatic differences in frequency of various haplotypes among Hispanics in different regions of the United States).

[FN75]. *Id*. at 5.

[FN76]. *Id*.

[FN77]. Yao et al., *supra* note 21, at 635.

[FN78]. *See id*. at 649:

> The comparison of the regional Han mtDNA samples revealed an obvious geographic differentiation in the Han Chinese, as shown by the haplogroups-frequency profiles.... Hence, the grouping of different Han populations into just "Southern Han" and "Northern Han" or the use of one or two Han regional populations to stand for all Han Chinese ... does not appropriately reflect the genetic structure of the Han.

[FN79]. *See, e.g*., David Biello, *Skulls Suggest Differing Stocks for First Americans* (Dec. 13, 2005), http://www.sciam.com/print_version.cfm? articleID=000E8538-F33D-139D-B33D83414B7F0000 ("Today, no South American native group presents the X [mitochondrial DNA] lineage, which is universal among North American native groups.") (alteration in original); Jason Eshleman et. al., *Mitochondrial DNA Studies of Native Americans: Conceptions*

and Misconceptions of the Population Prehistoric of the Americas, 12 EVOL. ANTHROPOL. 7-18 (2003) (noting that while Haplogroup X is found in low frequency in Europe and Western Asia, Native American variant is significantly different, possessing mutation that distinguishes it from Old World versions); Lynn B. Jorde & Stephen P. Wooding, *Genetic Variation, Classification, and "Race,"* 36 NATURE GENETICS S28, S29 (Nov. 2004) ("[I]ndividuals tend to cluster according to their ancestry or geographic origin."); Malhi et al. (2002), *supra* note 64, at 3-5 (stating native Americans have haplogroups whose frequencies varies greatly among Canada, United States, and Mexico); Esteban J. Parra, Rick A. Kittles et al., *Ancestral Proportions and Admixture Dynamics in Geographically Defined African Americans Living in South Carolina*, 114 AM. J. PHYS. ANTHROPOL. 118 (2001) [hereinafter Parra & Kittles (2001)]; Estaban J. Parra, Amy Marcini et al., *Estimating African-American Admixture Proportions by Use of Populations-Specific Alleles*, 63 AM. J. HUM. GENETICS 1839 (1998); Sarah A. Tishkoff & Kenneth K. Kidd, *Implications of Biogeography of Human Populations for "Race" and "Medicine,"* 36 NATURE GENETICS S21, S26 (Nov. 2004) (stating that frequency of mtDNA haplogroups are unevenly distributed within and among geographic regions and "knowledge of ethnicity (not just broad geographic ancestry) and statistical tests of substructure are important proper design of case control association studies"). *Cf.* Terry Melton et al., *Diversity and Heterogeneity in Mitochondrial DNA of North American Populations*, 46 J. FORENSIC SCI. 46 (2001) (arguing that North American population is homogeneous, and identifying, without exploring, population of Hispanics in Pennsylvania who differed significantly from any other population in study).

[FN80]. The authors' focus on the migration patterns of African Americans should not be taken as a statement that ancestry-related substructure in mtDNA profile distribution does not exist with respect to other groups in the United States. Rather, the focus reflects the fact that the African-American population exhibits high genetic heterogeneity, and the most infrequently occurring haplotypes, compared to other ethnic groups in the United States. As descendants of enslaved Africans, African Americans possess a diverse gene pool that is mainly of west and central African origin but also of substantial European and Native American admixture. As a result, it is of significant scientific importance, both in forensic science and biomedicine, to understand the genetic consequences of this unique population history. The authors' emphasis also reflects the significant number of studies on African-American migration in particular and the relative familiarity of the lay public with the historical post-slavery era migration of African Americans.

[FN81]. Rebecca L. Cann, Mark Stoneking, & Allan C. Wilson, *Mitochondrial DNA and Human Evolution*, 325 NATURE 31 (1987). *See also* Philip D. Curtin, *From Guesses to Calculations, in* THE ATLANTIC SLAVE TRADE: A CENSUS (David Northrup ed., 1994). Curtin's calculations were later refined by David Northrup. Paul E. Lovejoy, *Curtin's Calculations Refined but Not Refuted, in* THE ATLANTIC SLAVE TRADE 50-59 (David Northrup ed., 1994). *See also* Elizabeth E. Watson et al., *MtDNA Sequence Diversity in Africa*, 59 AM. J. HUM. GENETICS 437 (1996).

[FN82]. *See, e.g.*, Terry Melton et al., *Extent of Heterogeneity in Mitochondrial DNA of sub-Saharan African Populations*, 42 JOURNAL OF FORENSIC SCI 582, 588-89 (1997) (finding numerous haplotypes with occurrences of sequence-specific oligonucleotides (SSO) — particular base pair variations in certain parts of the mtDNA control region — of more than 10% in a particular African population and "substantial subpopulation heterogeneity" in "continental African populations"). The authors conclude that "control region sequencing would be a good alternative for forensic identifications in African or African-derived populations where there is uncertainty about whether subpopulations are present, at least until further populations are studied." *Id*. at 589.

[FN83]. *See generally* Salas et al., *supra* note 68, at 455-56.

[FN84]. Parra & Kittles (2001), *supra* note 79, at 19.

[FN85]. PHILLIP D. MORGAN, SLAVE COUNTERPOINT: BLACK CULTURE IN THE EIGHTEENTH CENTURY

CHESAPEAKE AND LOWCOUNTRY 33-44 (1998).

[FN86]. *Id*. at 34-36.

[FN87]. Fatimah Jackson, *Concerns and Priorities in Genetic Studies: Insights from Recent African-American Biohistory , 27 SETON HALL L. REV. 951, 961-62 (1997)*; Parra, Marcini et al., *supra* note 79, at 1839 (listing countries of Africa by economic region). This very same resistance makes African Americans whose ancestors come from the Gold Coast more likely to carry the sickle cell trait and sickle cell disease. A. Muniz et al., *Sickle-Cell-Anemia and Beta-Gene Cluster Haplotypes in Cuba*, 49 AM. J. OF HEMATOLOGY 163 (1995); Gabriella Pante-De Sousa et al., *Betaglobin Hapolytpes Analysis in Afro-Brazilians from the Amazon Region: Evidence for a Significant Gene Flow from Atlantic West Africa*, 26 ANNALS OF HUM. BIO. 365 (1999).

[FN88]. Curtin, *supra* note 81, at 83.

[FN89]. *See generally* JAMES R. GROSSMAN, LAND OF HOPE: CHICAGO, BLACK SOUTHERNERS, AND THE GREAT MIGRATION (1991).

[FN90]. *Id*. at 28-30.

[FN91]. *Id*. at 112-13 (describing migration from Mississippi delta to Chicago); NICHOLAS LEMANN, THE PROM-ISED LAND: THE GREAT BLACK MIGRATION AND HOW IT CHANGED AMERICA 119-20 (1991) (alluding to migration from Carolinas and Virginia up East Coast).

[FN92]. *See* http://www.censusgov/prod/cen2000/dp1/2khus.pdf (displaying a pictorial depiction of geographical distri-bution of African Americans in United States).

[FN93]. *See* Parra, Mancini et al., *supra* note 79, at 1845-47; Ranajit Chakraborty, *Gene Admixture in Human Popula-tions: Models and Predictions*, 29 YEARBOOK OF PHYS. ANTHROP. 1-43 (1986); David C. McLean, Jr. et al., *Three Novel MtDNA Restriction Site Polymorphisms Allow Exploration of Population Affinities of African Americans*, 75 HUM. BIOLOGY 147-61 (2003).

[FN94]. *See American, Indian, Eskimo, and Aleut Persons* (last visited Feb. 17, 2006) ht-tp://www.census.gov/geo/www/mapGallery/images/americanindian.jpg (displaying visual depiction of heavy Native-American clustering in western part of United States); STELLA U. OGUNWOLE, THE AMERICAN INDIAN AND ALASKA NATIVE POPULATION: 2000 4-6 (U.S. Census Bureau Feb. 2002) (noting that 43% of American Indians lived in West, 31% lived in South, 17% lived in Midwest, and 9% lived in Northeast United States).

[FN95]. Parra, Marcini et al., *supra* note 79, at 1845. The admixture study reports *two* results from Philadelphia, based on two independent sample sets taken from patients in two separate hypertension studies. These sample sets exhibited significant differences in their percentage of admixture. *Id*. Thus, even within a single city, different groups of African Americans display significantly different mtDNA profiles.

[FN96]. *Id*. at 1845-47.

[FN97]. *See* Carolina Bonilla et al., *Admixture in the Hispanics of the San Luis Valley, Colorado and Its Implications for Complex Trait Gene Mapping*, 68 ANNALS HUM. GENETICS 139, 140 (2004) (stating that the term "Hispanic" applies to individuals from several continents with "diverse cultural features and genetic back-grounds").

[FN98]. *See id*. (reporting differences in admixture among Puerto Rican, Cuban, and Mexican groups, as well as within smaller region of San Luis Valley).

[FN99]. *See* Bruce Budowle et al., *Population Data on the STR Loci D2S1338 and DI9S433*, FORENSIC SCI. COMM. (July 2001), *available at* http:// www.fbi.gov/hq/lab/fsc/backissu/july2001/budowle2.htm.

[FN100]. Ripan S. Malhi et al., *Native American MtDNA Prehistory in the American Southwest*, 120 AM. J. PHYS. AN-THROP. 108, 113 (2003).

[FN101]. *Id*. Additionally, the Navajo and Apache are not representative of the variation present in haplotypes/haplogroups among all North American Native Americans. Tribal groups in the United States share few haplotypes. *See* Malhi et al. (2002), *supra* note 64, at 914, tbl.2 (estimating sharing at about 29%).

[FN102]. Malhi et al., *supra* note 100, at 121-22.

[FN103]. The primary published analysis of this database concerns only the Chinese samples and while the analysis suggests that the frequencies of the haplogroups in the dataset are similar to those in another Han Chinese dataset of 263 individuals, the authors' data reveal significant differences in almost all cases. Marc W. Allard, Mark R. Wilson et al., *Control Region Sequences for East Asian Individuals in the Scientific Working Groups on DNA Analysis Methods Forensic MtDNA Data Set*, 6 LEGAL MED. 11, 18, fig.2 (2004). Other studies also show significant genetic variation among and within Asian populations. *See, e.g.*, Toomas Kivisild et al., *The Emerging Limbs and Twigs of the East Asian MtDNA Tree*, 19 MOL. BIOL. EVOL. 1737 (2002) (noting other Asian populations not represented in the SWGDAM East Asian database have significantly different frequencies of mtDNA haplogroups than those in the database); Terry Melton & Mark Stoneking, *Extent of Heterogeneity in Mitochondrial DNA of Ethnic Asian Populations*, 41 J. FORENSIC SCI. 591-602 (1996) (same); Yao et al., *supra* note 21, at 636 (combining all Han Chinese would be inappropriate).

[FN104]. *See* Terrance J. Reeves & Claudette E. Bennett, WE THE PEOPLE: ASIANS IN THE UNITED STATES, Pub. No. CENSR-17, U.S. Census Bureau, Dep't of Commerce 1, tbl.1 (2004) (listing major Asian groups in U.S., many of which are not included in SWGDAM Asian databases), *available at* http:// www.census.gov/prod/2004pubs/censr-17.pdf.

[FN105]. *Id*. at 4, fig. 1.

[FN106]. A chi-square analysis conducted by the authors comparing the SWGDAM and 2000 Census frequencies of Asian subpopulations (converted to sample sizes in both cases) rejects the hypothesis that the SWGDAM database is a random sample of the Census Asian Populations, with an extremely significant p value of less than 10^{-20}:

Asian Population	2000 Census	SWGDAM Database
Asian Indian	16.1%	2.4%
Cambodian	1.7%	0
Chinese	23.8%	45.7%
Filipino	18.3%	0

Hmong	1.7%	0
Japanese	7.8%	20.9%
Korean	10.6%	23.3%
Laotian	1.7%	0
Pakistani	1.6%	1%
Thai	1.1%	6.7%
Vietnamese	10.9%	0
Other Asian	4.7%	0

[FN107]. *See* Allard et al., *supra* note 34, at 1219-20.

[FN108]. *See* Wojciech Branicki, Ksenia Kalista et al., *Distribution of MtDNA Haplogroups in a Population Sample from Poland*, 50 J. FORENSIC SCI. 732, 733 (2005) (noting H Haplogroup was observed in 37.8% of samples in population from Southern Poland); Vincent Dubut et al., *MtDNA Polymorphisms in Five French Groups: Importance of Regional Sampling*, 12 EUR. J. HUM. GENETICS 293, 296 (2004) (showing that within France alone, frequency of H varies between 35% and 50% in two separate communities in Brittany); Ana M. Gonzalez et al., *Mitochondrial DNA Affinities at the Atlantic Fringe of Europe*, 120 AM. J. PHYS. ANTHROPOL. 391, 394 (recording 26.3% in Norway, 34% in England, 36.4% in Northern Germany, 38.5% in France and 42.2% in Galicia); Boris A. Malyarchuk et al., *Mitochondrial DNA Variability in Bosnians and Slovenians*, 67 ANNALS HUM. GENETICS 412-25 (2003) (illustrating frequency of H haplogroup is 24% in Finland, 26.8% in Scotland, and 45% in Poland). *See also* Pereira et al., *supra* note 21, at 7 (noting the use of SNPs to more closely examine haplogroups demonstrates significant inter-relatedness below the haplogroup level and suggests that "phylogenetic dissection of mtDNA haplogroups is revealing gradients previously hidden on the Eurasian scale").

[FN109]. That the SWGDAM database is not representative also arguably invalidates the FBI's use of a confidence interval to extrapolate from the database to a sub-population. Use of such margins of error presupposes random distribution in the population. WITTE, *supra* note 58, at 214.

[FN110]. *See* NRC II (1996), *supra* note 5, at 34 (noting that database of "a few hundred persons" is necessary even to have "some statistical accuracy" in estimating nDNA frequencies); RUDIN & INMAN, *supra* note 1, at 147 ("[T]he mtDNA databases are not yet large enough to be confident that an occurrence of a particular type divided by the number of people in the database gives a reasonable estimate of the frequency.").

[FN111]. Melton, *supra* note 79, at 46 and Budowle et al., *supra* note 51, at 31-32, argue that the SWGDAM database is valid based on the "lack" of significant population structure in the sequence-specific oligonucleotide ("SSO") types and

the similarity of the haplogroup frequencies in the database to various non-U.S. populations. This argument has two fundamental flaws. First, these studies look only to haplo*group* or SSO diversity, not to haplo*type* diversity, even though it is at the haplo*type* level that many population differences are detected and that the FBI generates its inclusion statistics. *See, e.g.*, Malhi et al. (2002), *supra* note 64, at 906. Second, their use of the F_{ST} — an ostensible measure of genetic population differentiation — is controversial. Melton (2001) relies on the F_{ST} to tout the homogeneity of North American populations. But the assumptions of F_{ST} make the statistic inherently biased against the detection of diversity among populations. Jeffrey C. Long & Rick A. Kittles, *Human Genetic Diversity and the Nonexistence of Biological Races*, 75 HUM. BIOLOGY 449, 450 (2003). Even if the use of F_{ST} indicates no significant subdivision in a haplogroup or SSO, such evidence is irrelevant to whether significant differences exist in frequencies of haplo*types* in various populations.

[FN112]. To calculate the cumulative probability that a database containing 1200 samples should miss a particular such profile, one must use the product rule to determine the probability that an event with probability .999 will not occur in 1200 trials. As it turns out, $(0.999)^{1200} = 0.301$.

[FN113]. *See* Tishkoff & Kidd, *supra* note 79, at S25. Of the 1771 individuals in the SWGDAM Caucasian database as of 2000, 72% of the profiles appeared only once in the database. Allard et al., *supra* note 34, at 1216; Parsons & Coble, *supra* note 15, at 305 (noting rare profiles exceed 50% of observed sequences in SWGDAM database). *See generally* Kittles & Keita, *supra* note 68, at 88-89.

[FN114]. *See, e.g.*, Carina Dennis, *Error Reports Threaten To Unravel Databases of Mitochondrial DNA*, 421 NATURE 773, 773-74 (2003) (reporting observation by Dr. Neil Howell that Dr. Forster's error-detection method may underestimate number of errors in databases); Forster, *supra* note 25, at 2:

> In forensics, accurate comparative mtDNA database are needed to assess the probability that an mtDNA profile from a crime stain is likely to derive from a suspect rather than from any other member of the population, so the number of errors in forensic journals listed in Table 1 does not engender confidence.

Corinna Herrnstadt et al., *Errors, Phantom and Otherwise, in Human MtDNA Sequences*, 72 AM. J. HUM. GENETICS 1585, 1585 (2003).

[FN115]. Hans-Jurgen Bandelt et al., *Detecting Errors in MtDNA Data by Phylogenetic Analysis*, 115 INT'L J. LEGAL MED. 64, 64 (2001).

[FN116]. *See, e.g.*, Hans-Jurgen Bandelt, Antonio Salas, & Lutz-Bonengal, *Artificial Recombination in Forensic MtDNA Population Database*, 118 INT'L J. LEGAL MED. 267 (July 2004).

[FN117]. Kevin Miller & Bruce Budowle, *A Compendium of Human Mitochondrial DNA Control Region: Development of an International Standard Forensic Database*, 42 CROATIAN MED. J. 315, 316 (2002). Miller and Budowle found that "a few substitutions in some published and SWGDAM sequences were clearly reviewed to be anomalous." *Id*. Sources for confusion in the data, according to the authors, include failure to conform to a standardized numbering system, non-recordation of insertions and deletions in the polycystine stretch of HVI, and differences between the number of sequences in the literature and the number of sequences in GenBank/EMBL. *Id*. While the authors subsequently recommended that the public data containing the errors be used for "investigative or research purposes only and not for the assignment of weight regarding forensic matches," the authors did not address how, if at all, the FBI addressed the SWGDAM sequencing errors. *Id*.

[FN118]. Hans-Jurgen Bandelt, Antonio Salas, & Antonio Bravi, *Problems in FBI MtDNA Database*, 305 SCIENCE 1402, 1403-04 (Sept. 2004).

[FN119]. *Id.*

[FN120]. *Id.*

[FN121]. *Id.*; Bruce Budowle et al., *Addressing the Use of Phylogenetics for Identification of Sequences in Error at the SWGDAM Mitochondrial DNA Database*, 49 J. FORENSIC SCI. 1, 1256 (Nov. 2004).

[FN122]. Budowle et al., *supra* note 121, at 1259 tbl.2, 1260 tbl.3.

[FN123]. *See* D. Michael Risinger & Michael J. Saks, *Rationality, Research and Leviathan: Law Enforcement-Sponsored Research and the Criminal Process*, 2003 MICH. ST. L. REV. 1023, 1047 & n.107 (2003) (noting that current FBI rules require an FBI employee to be a co-author on any article as a condition for gaining access to agency data).

[FN124]. AFDIL researchers have already suggested possible improvements to quality control in mtDNA testing. *See* Coble et al., *supra* note 21, at 139 Table (minimizing human intervention in process and reviewing all results by two individuals who conducted independent evaluations); Just, et al., *supra* note 23, at S148-49 (noting that implementation of a high-throughput robotic system for population databasing backed up by multiple scientists checking key laboratory steps increases the size and range of current mtDNA databases and decreases potential sources of error in creating databases).

[FN125]. *See, e.g.*, Pattern Jury Instr. (criminal cases) First Circuit § 3.02 (1998) ("It is a cardinal principle of our system of justice that every person accused of a crime is presumed to be innocent unless and until his/her guilt is established beyond a reasonable doubt. The presumption is not a mere formality. It is a matter of the most important substance."); Manual of Model Crim. Jury Instr. Eighth Circuit § 3.05 (2005) ("The presumption of innocence alone is sufficient to find the defendant not guilty and can be overcome only if the Government proves, beyond a reasonable doubt, each essential element of the crime charged."); Conn. Prac., Crim. Jury Instr. § 2.8 (3d ed. 2005) ("[T]he accused is presumed to be innocent until he is proved guilty. That means that at the moment when he was presented before you for trial, he stood before you free of any bias, prejudice or burden arising from his position as the accused."); Criminal Jury Instr. for the District of Columbia § 2.08 (2004) ("This presumption of innocence remains with the defendant throughout the trial unless and until s/he is proven guilty beyond a reasonable doubt."); Haw. Crim. Jury Instr. § 3.02 (2005) ("You must presume the defendant is innocent of the charge against him/her. This presumption remains with the defendant throughout the trial of the case, unless and until the prosecution proves the defendant guilty beyond a reasonable doubt."); Tenn. Pattern Jury Instr. Criminal § 2.01 (2005) ("This presumption [of innocence] remains with the defendant throughout every stage of the trial, and it is not overcome unless from all the evidence in the case you are convinced beyond a reasonable doubt that the defendant is guilty."); Va. Model Jury Instr. Crim. § 2.100 (2005) ("This presumption of innocence remains with the defendant throughout the trial and is enough to require you to find the defendant not guilty unless and until the Commonwealth proves each and every element of the offense beyond a reasonable doubt.").

[FN126]. Other commentators have advocated such modification to the counting method. *See* BALDING, *supra* note 68, at 99 ("to make some allowance for sampling variability, it is advantageous to include both the crime scene and the defendant profiles with those of the population database."); Marlan D. Walker, Note, *Mitochondrial DNA Evidence in State v. Pappas*, 43 JURIMETRICS J. 427, 437 (2003) ("[T]he fact that T has been observed once in a sample of 1220 individuals (the 1219 in the database plus the defendant) suggests that the sample frequency of 0/1219 used to form the confidence interval may be understated.").

[FN127]. Using the FBI's formula for calculating confidence intervals, *see* FBI MtDNA Protocols (2004), *supra* note 8, at § 11 at 10, the upper bound 95% confidence limit for 0/1148 is 0.26%. The upper bound 95% confidence limit for

2/1150 is still small, but almost twice as great, 0.42%. Using a more conservative 99% confidence interval increases the frequency estimates a bit more. The upper bound 99% confidence limit for 0/1148 is 0.4%. The upper bound 99% confidence limit for 2/1150 is 0.49%. The smaller the database, the more pronounced the effects of such modifications. The SWGDAM Chinese/Taiwanese population database has 356 profiles. The upper bound 95% confidence limit for 0/356 is 0.84%. The upper bound 95% confidence limit for 2/358 is 1.33%. Changing the confidence limits to 99% causes the upper bound confidence limits increase to 1.3% and 1.6%, respectively. While the practical effects of these modifications may be marginal in most cases, the difference may be material in a particular case, and accuracy is a worthy goal in itself.

[FN128]. Frye v. United States, 293 F. 1013 (D.C. Cir. 1923).

[FN129]. *Id.* at 1014:

Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential force of the principle must be recognized, and while courts will go a long way in admitting expert testimony deduced from a well-recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field in which it belongs.

[FN130]. Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

[FN131]. *Id.* at 589. The *Daubert* test was subsequently refined by the Court and incorporated into the relevant Federal Rule of Evidence. *See* Kumho Tire v. Carmichael, 526 U.S. 137, 138 (1999) (extending *Daubert* more generally to non-scientific expert testimony); General Electric Co. v. Joiner, 522 U.S. 136, 136-37 (1997) (applying abuse-of-discretion standard of review to trial court's determination of admissibility under *Daubert*); Comment to Fed. R. Evid. 702 (discussing 2000 amendments to Federal Rules of Evidence in response to *Daubert* that codify the requirement that "the testimony is the product of reliable principles and methods" and that "the witness has applied the principles and methods reliably to the facts of the case").

[FN132]. *See generally* Andrew R. Stolfi, Note, *Why Illinois Should Abandon Frye's General Acceptance Standard for the Admission of Novel Scientific Evidence*, 78 CHI.-KENT L. REV. 861 (2003) (discussing standards for admission of scientific evidence in all U.S. jurisdictions).

[FN133]. People v. Pizarro, 3 Cal. Rptr. 3d 21, 44 (Cal. Ct. App. 2003); United States v. Porter, 618 A.2d 629, 633-34 (D.C. 1992).

[FN134]. *See* MICHAEL J. SAKS ET AL., ANNOTATED REFERENCE MANUAL ON SCIENTIFIC EVIDENCE, SECOND 73 (2004) (stating that "*Frye* is often criticized as overly conservative, for it imposes a protracted waiting period that valid scientific evidence and techniques must endure before gaining legal acceptance.").

[FN135]. *Daubert*, 509 U.S. at 592-93.

[FN136]. *Id.* at 593-94.

[FN137]. *Id.* at 597-98.

[FN138]. *See id.* (stating that "[p]ertinent evidence based on scientifically valid principles" satisfies the Federal Rules of Evidence).

[FN139]. *See* SAKS ET AL., *supra* note 134, at 78 & n.9 (listing jurisdictions that have adopted or declined to reject *Daubert*).

[FN140]. *See* BUTLER, *supra* note 12, at 270 ("When 'failure to exclude' is the interpretation for reference and evidence samples, then a statistical estimate of the significance of a [mtDNA] match is needed."); *Porter*, 618 A.2d at 640 (indicating that a statistical assessment of significance of DNA is at the core of its admission and "underlying method of arriving at that calculation must pass muster under [*Frye*]"). *See generally* Kaye & Sensabaugh, *supra* note 5, at 545 & n.269 (noting a number of courts that have concluded that reliable statistical methodology must accompany science to be admissible). *But see id*. at 546 & n.275 (advocating that jurors need not be presented with a particular number if the profile is shown to be exceedingly rare by admissible scientific methodology).

[FN141]. This point should not obscure forensic mtDNA testing's effectiveness in the exoneration of suspects. The issue when *excluding* an individual is simply whether the sequencing was done properly at each stage. But when mtDNA typing is used to *include* an individual as a suspect, the information has no meaning without determining the statistical significance of the inclusion.

[FN142]. *See* SAKS ET AL., *supra* note 134, at 96-97 (comparing *Daubert* and *Frye* tests).

[FN143]. One dilemma facing courts is whether to consider the defendant's apparent ancestry in determining which database to use to determine a frequency estimate. At least one court has suggested that the presumption of innocence requires that no assumptions be made as to the perpetrator's ancestry and, thus, the statistics reported to the jury should not assume that the perpetrator is of a particular ancestry. *See, e.g*., People v. Prince, 36 Cal. Rptr. 3d 300, 305-07 (Cal. App. 5th Dist. 2005) (reaffirming and following *Pizarro*'s disapproval of how the prosecution, when it presented the Hispanic profile frequency, impermissibly assumed the *perpetrator*, like the defendant, was Hispanic). On the other hand, where a perpetrator is likely from a particular ethnic community, it may be to the defendant's advantage to consider the perpetrator's ancestry, because the observed haplotype may be quite common in a particular ancestral sub-population, even though very uncommon in the general U.S. population. *See* Julian Adams, *Nuclear and Mitochondrial DNA in the Courtroom*, 13 J. L. & POL'Y 69, 88 (2005) (giving example of *Passino* case in which perpetrator of crime in remote trailer camp was likely of Abnaki ancestry).

[FN144]. In December 2003, the Public Defender Service for the District of Columbia commissioned a jury poll through Lake Snell Perry and Associates, an independent polling firm, of 1000 potential D.C. jurors. *See* http://www.pdsdc.org/SpeciaILitigation/SLDSystemResources/Brady%20Poll%CCC20Results,%CCC20December%CC0 C 03.pdf. The poll showed that, on a scale of 0 to 10, 10 being most persuasive, the mean response for DNA evidence was 9, as compared to 6.6 for the testimony of the accuser. *Id*. at 2. Thirty-one percent of those polled stated that DNA evidence can never "be wrong." *Id*. at 4. Thirty percent stated that mistakes are made "almost never" with respect to DNA evidence. *Id*. When asked which was more reliable, nuclear or mtDNA, 32% answered that the two forms of DNA are "equally" reliable, while 11% answered that mtDNA was *more* reliable. *Id*. A study commissioned by the National Institute of Justice showed that, after sitting through a mock trial involving mtDNA, a large percentage of jurors fell victim to fallacies and misperceptions about DNA in general, and mtDNA in particular. *See generally* B. MICHAEL DANN ET AL., TESTING THE EFFECTS OF SELECTED JURY TRIAL INNOVATIONS ON JUROR COMPREHENSION OF CONTESTED MTDNA EVIDENCE, FINAL TECHNICAL REPORT 41-54 (Dec. 30, 2004), *available at* http://www.ncjrs.gov/pdffiles1/nij/grants/211000.pdf. *Cf*. Michael J. Saks & Jonathan J. Koehler, *The Coming Paradigm Shift in Forensic Identification Science*, 309 SCIENCE 892, 893 (2005) ("[E]rroneous forensic science expert testimony is the second most common contributing factor to wrongful convictions, found in 63% of those cases.").

[FN145]. For state courts that have admitted mtDNA evidence under *Frye*, see Magaletti v. State, 847 So. 2d 523, 526-29 (Fla. Dist. Ct. App. 2003); Wagner v. Maryland, 864 A.2d 1037, 1044-50 (Md. Ct. Spec. App. 2005); People v. Holtzer, 660 N.W.2d 405, 409-11 (Mich. Ct. App. 2003); People v. Ko, 757 N.Y.S.2d 561, 563 (N.Y. App. Div. 2003); People v. Klinger, 713 N.Y.S.2d 823, 831 (N.Y. Sup. Ct. 2000). *See also* Adams v. State, 794 So. 2d 1049, 1057 (Miss. Ct. App. 2001) (stating in one sentence that mtDNA expert was qualified and that, because expert claimed evidence was "generally accepted," defense challenge to testimony was denied). *Contrast* RUDIN & INMAN, *supra* note 1, at 195 (reporting on *State v. Crow*, No. 96-1156 (Fla. 18th Cir. Ct. May 14, 1998), in which the trial judge "ruled that the results of an mtDNA test did not meet the *Frye* standard and were inadmissible as evidence. He based his opinion on his understanding that the FBI database was too small and was insufficient to provide reliable statistical conclusions. [The judge] further found that the 'counting method' failed to provide meaningful comparison that would assist, rather than confuse, the jury.")

[FN146]. For federal courts that have admitted mtDNA under a *Daubert* standard, see United States v. Beverly, 369 F.3d 516, 527-31 (6th Cir. 2004); United States v. Coleman, 202 F. Supp.2d 962 (E.D. Mo. 2002). For state courts that have admitted mtDNA under a *Daubert* standard, see Lewis v. State, 889 So. 2d 623, 668-74 (Ala. Crim. App. 2003); State v. Pappas, 776 A.2d 1091, 1100-13 (Conn. 2001); State v. Underwood, 518 S.E.2d 231 (N.C. App. 1999); State v. Council, 515 S.E.2d 508 (S.C. 1999). *Cf.* State v. Scott, 33 S.W.3d 746, 759-60 (Tenn. 2000) (admitting mtDNA evidence by statute that looks at reliability of proposed evidence).

[FN147]. *See Beverly*, 369 F.3d at 530-31 (stating court heard only from prosecution's expert); *Lewis*, 889 So. 2d at 673-74 (same); *Magaletti*, 847 So. 2d at 526-27 (same); *Klinger*, 713 N.Y.S.2d at 824 (same); *Scott*, 33 S.W.3d at 752 (upholding denial of hearing as not abuse of discretion and deeming harmless trial court's failure to give defendant funds to hire DNA expert).

[FN148]. The Public Defender Service for the District of Columbia raised many of the issues discussed in this Article through testimony, affidavits, and articles from statisticians, genetic anthropologists, molecular biologists, and population geneticists at a *Frye* hearing in D.C. Superior Court in July 2004. While the trial judge admitted the mtDNA evidence, the jury rendered a verdict of not guilty on all counts — perhaps reflecting the exculpatory nature of some of the mtDNA evidence and/or the challenges to the prosecution's frequency statistics brought out at trial. *Compare* Memorandum & Order, United States v. Chase, No. F-7730-99, 2005 WL 757259 (D.C. Super. Jan. 10, 2005) (denying defendant's motion to exclude mitochondrial DNA test results in the Ida Chase case), *with* Henri E. Cauvin, *Woman Acquitted in 1996 Slaying of Md. Salesman*, WASH. POST, Feb. 10, 2005, at B01 (reporting Mrs. Chase's acquittal).

[FN149]. *See, e.g.*, Adams, *supra* note 143, at 87-89 (focusing on heteroplasmy issues; touching upon potential relevance of perpetrator's ancestry in determining mtDNA frequency estimate); Kiran Bisla, *It All Came Down to a Single Hair: The Probability of Exclusion vs. the Probability of Guilt Through the Use of Mitochondrial DNA Evidence in* State v. Pappas, 26 WHITTIER L. REV. 263, 296-98 (2004) (analyzing *Pappas* decision and briefly noting that court dismissed arguments relating to convenience samples and fact that "FBI was in complete control of the contents of the database"); Edward K. Cheng, *Mitochondrial DNA: Emerging Legal Issues*, 13 J. L. & POL'Y 99, 107-18 (2005) (focusing on advantages of mtDNA testing over microscopic hair analysis and on privacy issues in mtDNA databanks); Paul C. Giannelli, *Mitochondrial DNA*, 19 CRIM. JUST. 54, 54-56 (Winter 2005) (primarily discussing problems with contamination and chain of custody); FAIGMAN ET AL., *supra* note 4, at § 25 (discussing legal and scientific issues with DNA typing).

[FN150]. *See, e.g.*, Pereira et al., *supra* note 21, at *2 (study is "an attempt to extend the use of phylogeographic approaches to mtDNA forensics"); RUDIN & INMAN, *supra* note 1, at 196 ("Forensic scientists tend to be insular and

self-reliant to a fault.").

[FN151]. Mildred K. Cho & Pamela Sankar, *Forensics Genetics and Ethical, Legal, and Social Implications Beyond the Clinic*, Vol. 36 No. 11 NATURE GENETICS SUPP. S-8, S-9 (Nov. 2004).

[FN152]. SAKS ET AL., *supra* note 134, at 78.

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