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Policy Implications of Defining Race and More by Genome Profiling

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Abstract

The genome revolution has provided the basis for many new applications in diverse areas such as health, food and agriculture, and forensics. While standard DNA profiling has become the paramount form of identification in forensics, expansion of genomic applications is being considered and tested to provide more descriptive information to facilitate the capture of perpetrators. Two major applications are being explored and tested: 1) ancestry profiling from which race can be inferred; and 2) profiling for physical traits to provide a genetic-based description or sketch. The use and incorporation of these new applications raises several logistical questions and ethical issues. This article will explore some of the policy implications in the use of expanded genome profiling for forensics purposes.

Introduction

The discovery that every person carries a unique molecular signature that can be detected in virtually every human tissue was a major boon to crime scene investigators.[1,2] Almost a decade prior to the completion of the sequencing of the human genome, DNA fingerprinting became the identification tool of choice following the standardization of a core panel of DNA markers and development of local, state/regional, national and international databases.[3] Now, with the wealth of advances in genomic technologies and a much greater understanding of human genetic variation, molecular forensics is potentially on the cusp of another revolution.

Whereas the genetic similarity between humans was heavily emphasized upon completion of the Human Genome Project, the follow-up project of the HapMap instead focused on genetic variation of individuals from different populations.[4] The impetus for defining genetic variation among populations was to facilitate the identification of genes and variations functionally relevant to human health and disease. However, other applications of genetic variation have arisen from the enormous datasets now available. There are at least two forensic applications using genome profiling. First, genetic variation between populations can be used to determine ancestry. Race can then be inferred, with debatable accuracy, from a prediction of ancestry. A second application and newer approach in forensics is the application of genetic knowledge of physical or behavioral traits to develop a composite sketch of an individual based solely on genetic information.

Predicting race and an individual's appearance based on genetic information presents some ethical and moral issues that warrant careful consideration before these technologies are used routinely. This paper will review some of the science of genome profiling applied for forensic uses and discuss several of the policy implications arising from this new technology.

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Genome Profiling to Predict Ancestry and Race

All of the DNA contained in a single cell comprises what is known as the human genome. DNA is actually a chemical composed of four units, abbreviated A, T, C, and G. The human genome contains three billion units strung together. The three billion units are arranged into large packages known as chromosomes which are visible under a microscope. Humans have 24 chromosome pairs numbered one thru 22, plus a pair of sex chromosomes (XX in females and XY in males). Half of the chromosome pair is inherited from the mother and half from the father.

It is the order of the units, or sequence, that is critical for normal development, growth and functioning. Humans are 99.9 percent identical in their genome sequence and genes are made of distinct regions of DNA sequence. The remaining 0.1 percent difference accounts for human diversity. Studies of human genetic variation or alterations in the sequence of DNA units or structure of chromosomes, can vary depending on the type and location of variation. For example, variation may occur in regions of DNA that do not encode for genes located on either the X or Y chromosome.

Another type of variation involves short sequences that are repeated in tandem, known simply as short tandem repeats (STRs). The standardized forensic DNA profile is composed of a set of core STRs found throughout the human genome in non-coding regions. Each individual has a varying number of repeats at each of the sites. For example, one individual may have four STRs (ATCG) at one site while another individual has nine (ATCG) repeats. No additional information such as health risks or appearance can be gleaned from the standardized DNA profile (purposely so).[5] Although not part of the standard analysis, a weak correlation has been shown between some of the STR markers and racial groups.[6]

There has been substantial interest in developing DNA profiles that may provide more descriptive information from biological specimens left at a crime scene. In particular, this information would be useful in criminal investigations to identify and apprehend perpetrators as quickly as possible and before further crimes can be committed. Data collected from studies of human genetic variation may be applicable to these purposes. Population genetic studies using particular DNA variants (referred to as markers) have enabled clustering of individuals into groups that correspond to geographic or ancestral origin.[7] About 93 to 95 percent of human genetic variation is found *within* populations with most of the remainder corresponding to variation *between* populations.[8]

DNA markers with wide frequency differences between populations have been used to infer ancestry.[9] For example, a panel of these variants – known as 'ancestry informative markers' or AIMs – have been used to predict proportions of an individual's ancestry – e.g., 80 percent African and 20 percent European or 10 percent Asian and 90 percent European.[10,11] Using these markers, several companies have been launched to provide ancestry information to interested individuals and law enforcement agencies. For example, DNAPrint Genomics has offered ancestry genotyping services to law enforcement agencies including Canadian law enforcement agencies, the U.S. Federal Bureau of Investigation, Scotland Yard, and the U.S. Army.[12]

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Whereas ancestry confers origin, race is a socially defined concept. The concept of race is derived from a historical division of the human population. In the 18th century, Carl Linnaeus defined four 'types' of humans: Americanus, Europaenus, Asiaticus, and Africanus.[13] These divisions were primarily determined by geography/origin and physical features such as skin pigmentation, hair texture, and nose shape (see Figure).

Figure 1. The cover of Linnaus' book (http://www.linnaeus.uu.se/online/animal/1_1.html). The table summarizes the descriptive features of populations.


CAROLI LINNÆI
SYSTEMA
NATURÆ
NATURÆ REGNA TRIA,
SECUNDUM
STOCKHOLMIÆ
Apud GOTTFR. KIESEWETTER.

Europeaeus	skin (white); build (muscular); hair (long, flowing), eyes (blue); disposition (gentle, and inventive)
Americanus	skin (reddish); build (erect); hair (black, straight, thick); distinct facial features (wide nostrils); disposition (stubborn and angered easily)
Asiaticus	skin (sallow; yellow); hair (black); eyes (dark); disposition (avaricious and easily distracted)
Africanus	skin (black); hair (black, frizzled); skin texture (silky); distinct facial features (nose flat, lips tumid); disposition (relaxed and negligent)

Although studies have shown a high correlation between genetically-defined ancestry and self-identified race,[14] predicting an individual's race based on these markers still involves some guesswork. In populations where admixture is high, the ability to predict race will likely be reduced (admixture refers to the mixing of one or more populations). For example, many individuals from countries in Central America and the Caribbean have a three-part heritage: Native American, European, and African. The individual's place of residence, where they were raised, and culture will certainly influence the race they self-identify with which cannot be revealed through DNA analysis. However accurate though, a descriptor such as 'perpetrator's ancestry believed to be 80% Northern European and 20% Native American' is not likely to be used in an All Points Bulletin.

Genome Profiling to Predict Physical Appearance

For investigatory purposes, knowing an individual's race can help narrow down the field of suspects or the population of individuals sought for a crime. However, knowing an individual's race can be misleading if used to predict certain physical traits. What exactly does someone look like who has a mixed background of European, sub-Saharan African, and Native American genetic markers? For companies like DNAPrint, since a unique description cannot be predicted based on a given ancestry profile, a collection of photographs is provided of what a person with a

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particular ancestry profile *might* resemble. Although two people can have the same ancestry profile, it does not mean that they will share all of the same physical features. For even one physical trait, the data have been conflicting regarding the strength of the relationship between skin color and genetically-defined ancestry.[15,16] Just as admixture can confound the prediction of race, admixture can present challenges for the prediction of general physical appearance. Therefore, a substantial gap remains between ancestry and/or race and physical appearance.

In addition to the core DNA profile, markers on the X and Y chromosome are routinely run to determine gender, an obvious genetic trait. This is the only physical trait that can be easily revealed through DNA analysis today. An expanded genome profile of other physical traits could provide further details to assist in the identification of the perpetrator. Advances in developmental and medical genetics have identified genetic variations associated with physical traits that may be applied for law enforcement purposes. For example, data gleaned from genetic studies on diseases with abnormal skin pigmentation or certain developmental features (e.g., head circumference, height, hair texture) could be applied to predict certain physical characteristics of an unknown individual.

Imagine a description of a perpetrator obtained solely from blood spatter found at a crime scene:

> *'Suspect is believed to be a male Caucasian with blue eyes, straight brown hair (possibly thinning), light to medium skin color, and likely to be overweight with an aggressive personality.'*

While this is far from a perfect description, it may considerably reduce the field of suspects. Realistically, it is unlikely that genomic data can provide such definitive descriptions given the complexity of gene-gene and gene-environment interactions that probably contribute to the development of both physical traits and behavior. But while the data to support this type of genetic-based description are mostly weak as described below, the potential exists and companies are investing in research to develop these expanded genome profiles.

Skin pigmentation

To begin, differences in skin pigmentation span a continuum of color across human populations. Variation in skin, hair, and eye color is attributable to virtually one pigment known as melanin.[17] Two distinct types of melanin are produced: black/brown pigments are produced by eumelanin and red/yellow pigments produced by pheomelanin. Each melanocyte (melanin-producing cell) has the capacity to synthesize both types of pigment. Melanin is secreted to surrounding hair follicles or is retained by melanocytes of the eye. Melanin is synthesized within specialized intracellular organelles known as melanosomes. Differences in the number, size, and distribution of melanosomes are observable between ethnic groups.

Several genes are known to be involved in the production of melanin (see Table 1). For example, of nine common variation in a gene known as MC1R, three have been associated with fair skin and red hair and are absent in the African population. A study

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of 859 Caucasian individuals reported that all 71 redheads carried at least one MC1R variant and >60% carried two or three variants.[18] Interestingly, 34% of individuals carrying two red hair color markers were *not* redheads. A recent paper reported an association between a variant in the gene SLC24A5 and lighter skin color in admixed populations.[19]

Table 1. Select genes associated with certain physical traits

Trait	**Genes/Chromosomal regions**
Skin pigmentation	TYR, TYRP1, TYRP2, P, MC1R, SLC24A5
Eye color	Chromosome 15 and 19, P, ASIP
Hair color/texture/loss	MC1R, MATP, FS, TGFA, EGFR, KRN1 (keratins)
Body shape	TBX15, GPC4, and HOXA5

Eye Color

Given the vastness of the human genome, it is a major challenge to identify the key gene or genes responsible for a certain trait or disease. As a first step, scientists may attempt to narrow down which chromosome the causative gene may reside. This approach would be analogous to finding a perpetrator – given a city, the first step would be to identify the likely neighborhood the person lives or works. With respect to eye color, several studies have identified certain chromosomal regions where putative eye pigmentation genes may reside. Chromosome 19 has been linked to blue or gray eye color[20] and chromosome 15 to brown or blue eye color.[21],[22],[23] A subsequent study of 629 individuals found that persons carrying particular genetic variants in a gene known as the P gene on chromosome 15 were less likely to have blue or gray eyes.[24] Another study of 502 twin families confirmed the link between 15q and eye color.[25] A variant in the ASIP gene in the melanin pathway has also been associated with dark hair and brown eyes in European-Americans.[26]

Hair Color/Texture/Loss

Hair growth rate, texture, color, and shape differ between individuals; however, some hair characteristics are associated with certain population groups. For example, Asian hair is on average the thickest and most coarse hair type compared to Caucasian and African-American hair. Obviously, if hair samples are left behind at a crime scene, information can be gleaned without the need for genetic analyses.

Factors such as light, hormones, temperature, nutrition, and genetics affect various hair characteristics. Current understanding of genetic polymorphisms linked to hair color, structure, or alopecia (hair loss) is weak. As mentioned above, the relationship

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between red hair/fair skin and genetic variants in MC1R has been reproduced and validated.[27,28] Other studies have demonstrated associations between the gene MATP and dark hair, skin, and eye color in Caucasians.[29]

Several genes have been implicated in the regulation of hair follicle development or control of hair growth cycle.[30] Of the genes known to be involved in follicle development or hair growth, only a few mutations have been associated with abnormal follicle shape and wavy hair. Variations in keratins, proteins present in hair and nails, have been identified in Japanese and Caucasian individuals, indicating the occurrence of genetic variants that are highly specific to a certain population.[31]

Another hair trait is male pattern baldness. Despite its name of male pattern baldness, it is also the most common form of hair loss in females. The frequency of baldness varies between populations, effecting between 50 and 80 percent of Caucasian men but half as common in Chinese, American Indians, and African-Americans. The frequency of baldness increases with age in men but not women. Although presumed to result from a genetic predisposition (yet to be defined), differences in trait frequency between populations have also been attributed to diet, smoking, and disease.

Other Traits

For other physical traits, less is known about the biological pathways and genes. While many genes are known to be involved in bone growth and development, genes related to bone and tissue structure are even less certain, such as nose, ear, cheek or eye shape. Identifying genes associated with other morphological features would thus require a considerable amount of new research, but would likely provide only vague descriptions at best due to environmental influences.

The MC1R gene accounting for red hair color and fair skin has also been linked to freckles.[32] In addition to facial features, genes have been linked to small head size,[33,34] obesity,[35,36,37] height,[38,39] and other such descriptive characteristics. Genes involved in fat distribution that may be useful in predicting body shape, such as hourglass, pear, or apple shape, were recently elucidated.[40]

Beyond appearance, an increasing amount of study has focused on the genetics of behavior. Behavior is likely to be more complex than the all of the physical traits combined given the influence of lifestyle, family, culture and other factors. Several genetic variations have been associated with traits such as shyness,[41,42] novelty-seeking,[43,44] and aggression and violence.[45,46]

A Slippery Slope

In comparison to the quantitative preciseness and accuracy of the core STR DNA identification profile, AIMs and genetic markers associated with ancestry and physical or behavioral traits appear to be far less reliable for identification purposes. Regardless of the validity of this technology or whether it will be useful to forensic investigators, expanded genome profiling will pose major challenges in its use. To begin exploring some of these challenges, I describe several procedural and logistical

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issues in the investigative format of who, what, when, where, and how. The discussion is limited to the use of an expanded genome profile for unidentified biological specimens collected from crime scenes. Not surprisingly, many of the responses to the practical questions regarding the appropriate use of an expanded genome profile are influenced by ethical issues.

Who?

The first question and likely the most difficult question to be addressed is the issue of who, or more precisely for which crimes, should undergo expanded genome profiling. This same question was also one of the first questions encountered during the initial use of the core DNA profile.[47] In the U.S., only those convicted of sexual crimes or other violent crimes were profiled and their information stored in DNA databases. In 1990, the FBI Laboratory's Combined DNA Index System (CODIS) was initiated as a pilot project in 14 states. The FBI's authority to establish a national DNA index for law enforcement purposes was codified in the DNA Identification Act of 1994.[48] In 1998, the FBI's National DNA Index System (NDIS) became operational, enabling laboratories across the country to exchange and compare DNA profiles. The most recent statistics from NDIS indicate that more than 2.8 million profiles are stored in the database, 96 percent belonging to convicted offenders.[49]

The type of crimes for which the core DNA profile was required and stored gradually expanded to include all felonies, juvenile offenders and all arrestees even if not convicted.[50] This expansion was due in part to technological advances enabling DNA extraction and profiling from very small biological samples in addition to the often more plentiful blood and semen samples left behind at crime scenes.[51]

But who exactly would an expanded genome profile be ordered for? Only specimens from unsolved crimes would benefit from an expanded genome profiling, but would this include all crimes or be reserved for sexual or other violent crimes? Should a tiered approach be used where all specimens from heinous crimes of murder and rape as well as other crimes committed multiples times be automatically tested for an expanded genome profile, followed by all crimes unsolved for some specified period of time such as three months? Or, regardless of the crime, should all biological specimens left behind at a crime scene be subject to expanded genome profiling?

Specific criteria will be needed to determine which samples collected from crime scenes will be tested for an expanded genome profile and at what stage of the investigation. However, several issues need to be considered in the construction of such a policy. First, what are the benefits and risks of using expanded genome profiling for some or all crime scene specimens? The obvious benefit is that expanded genome profiling would lead to the more rapid apprehension of the perpetrator. However, while this assumption seems logical, there is no evidence to support this. If a pilot project is initiated, data could be collected retrospectively and compared to police statistics on time to apprehension prior to the use of expanded genome profiling. This data will also be important in demonstrating the cost-effectiveness of this new technology. Although technology is rapidly advancing resulting in reductions of the amount of specimen needed, cost per assays and turnaround time, depending on the policy, new expenses and burdens will inevitably be incurred on forensic laboratories.

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Second, in determining who or for which crime expanded genome profiling should be conducted, the impact of expanded profiling on a defined group of individuals must be considered. The present make-up of DNA databases suggests proceeding very cautiously with expanded genome profiling. In Britain, the profiles of 4 in 10 black men compared to 1 in 10 white men are stored in the world's largest national police database.[52] If we assume that the number of unsolved crimes will follow the criminal statistics of solved and convicted crimes, the issue of racial profiling based on genetic make-up becomes a significant concern.

One of the fears is that expanded genome profiling will lead to reification of the belief of the biological basis of race. In particular, the use of expanded genome profiling may lend credence to the opinion that criminal activity is associated with a particular genetic make-up prevalent in certain races and/or individuals. This concern is not without precedence. During the 1960's and 1970's, it was found that institutionalized or incarcerated men had a higher prevalence of an extra Y chromosome than non-incarcerated men, leading to the development of an unsupported stereotype of these individuals – 'tallness, low IQ, a behavior disability, and nodulocystic acne.'[53] Subsequent studies could not conclusively demonstrate that the extra Y chromosome was linked to aggressive or violent behavior.[54,55,56] Race was not associated with the extra Y chromosome, although the racial make-up of incarcerated men at that time is very different from today. But the experience from this work illustrates how quickly unsupported stereotypes can arise, setting the precedent for associating genotype and criminal behavior. Therefore, it is difficult not to wonder whether expanded genome profiling will follow a similar path.

Ancestry testing may provide more definitive information about an individual's heritage beyond the self-identified race/ethnicity categories commonly used. While this may be informative from a scientific or personal interest perspective, it may or may not be useful in providing additional information about the perpetrator's identity. Beyond the race/ethnicity statistics of convicted criminals, ancestry data may provide more definitive (and biological) links between criminal behavior and ancestry. As there are no pure populations, everyone is a mixture of populations and groups. If it were possible to identify one or more ancestral markers linked to criminal behavior that cut across race/ethnicity categories, that could result in the creation of a new type of profile but one that would not be obvious without testing. Therefore, the association would not be useful in deciding which vehicles to stop for a traffic violation, but might be predictive of criminal behavior.

So, how likely would it be for a genetic marker or genetically-defined trait to be associated with individuals of a certain race or ethnicity? First, an individual or group would need to conduct research to ascertain this relationship. If the actual sample collected from the crime scene as well as the result from the genome profile were destroyed after the perpetrator was apprehended and tried, this would make it next to impossible to establish an association between race and a behavioral trait. Nevertheless, it is certainly possible for a researcher to study the genetic make-up of ex-incarcerated individuals independent of data collected from forensic analysis. However, the data would likely fail to be replicated given the complexities of defining the genetic and environmental components of behavior, the latter of which is believed to play the bigger role.

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If certain genetically-defined traits were associated with criminal behavior, irrespective of race/ethnicity, it is quite possible that this data could be used to screen individuals to ascertain the likelihood of committing criminal acts. A number of scenarios could be envisioned – screening may be available to parents of newborns, children with unruly or aggressive behavior, or those that have committed misdemeanors; to school administrators; to prospective adoptive parents; or to employers. Regardless of how weak the predictive test result might be, individuals testing positive would most likely experience some form of discrimination. As all of these scenarios would not involve police or forensic investigators, this will be a major issue for society to address about the use of genetic screening for behavioral traits. Given some of the market strategies enabling consumers to directly order genetic tests for ancestry, paternity, and some health conditions, it is not outside the realm of possibility that these types of tests would be next to be offered.

Despite the low likelihood of identifying an association between genes, race, and criminal behavior, this fear will likely linger given that populations have been discriminated and stigmatized based on genetic make-up (e.g., sickle cell anemia and African-Americans). Developing a policy that specifically defines for which crime(s) the samples will be tested and calling for the destruction of both the sample and expanded genome profile results following apprehension and trial of the perpetrator will be critical to minimizing abuses. Secondly, educating the public about how these profiles will be used to aid criminal investigations and the safeguards that will be put in place will be equally important in allaying fears. As will be discussed in the next section, the issue of what to test in an expanded genome profile will be critical to avoiding potential associations between a certain genetic make-up and trait/behavior or crime. For example, knowing the behavioral characteristics of a person who has already committed a crime may not be as helpful in finding and apprehending a suspect as knowing certain physical features.

Lastly, one of the most common concerns of DNA profiling is the potential violation of privacy. There appears to be a sliding scale of privacy rights with respect to DNA profiling. Biological specimens left at crimes scenes are often considered abandoned property and therefore, privacy rights of the specimen do not exist. Convicted criminals have fewer rights than arrested individuals or suspects, and arrested individuals or suspects have fewer rights than innocent individuals. Since the type of profile discussed here only pertains to abandoned crime scene specimens, there would not be any privacy violations if the expanded genome profile was performed solely for the purposes of acquiring additional descriptive information about the perpetrator and subsequently destroyed upon apprehension.

The concern comes into play, however, when the expanded genome profile provides information beyond descriptive features that are then attached to the perpetrator once their identity is known. An expanded genome profile that reveals information about health and behavioral traits would present a much greater violation of personal privacy than the core DNA profile or an expanded profile for physical features. Therefore, the discussion on what to profile is intimately linked to the privacy concerns. The potential disclosure of health and behavioral information would likely constitute a major violation of 'informational privacy.'[57] Since many genes are

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associated with multiple traits and conditions, privacy violations must be weighed against public safety for genetic information that may unintentionally reveal additional information about other traits such as a medical condition.

Another privacy concern relates to family members. Given the inherited nature of the information, expanded genome profiling can potentially reveal information about the perpetrator's family members. Even for health applications of genetic testing, the disclosure of genetic test results to relatives has been the subject of substantial debate.[58,59] Again, if the sample and information gained from expanded genome profiling is destroyed upon identification and apprehension of the suspect, privacy violations of family members will be substantially minimized. Only the core DNA profile will be needed and stored to confirm the identity of the perpetrator to the crime scene specimen.

One factor that may address many of the concerns raised about whom or for what crime an expanded genome profile would be ordered is the creation of a universal database. If a core DNA profile is obtained and stored in a national database from everyone at birth, an expanded genome profile would only be beneficial if the perpetrator was not in the database, such as that of a person visiting or recently moved from another country.

What?

The next question is what exactly will be profiled. Ancestry profiles from which race can be inferred have been available for the past few years. However, as genomics research continues to uncover the link between genetic variation and physical and behavioral traits, which traits should be included in an expanded genome profile? Can these expanded profiles be standardized like the core STR profile? At present, the novelty and dynamics of the field will likely not permit standardization for the foreseeable future. If the technology can be validated and demonstrated to be useful in different groups across the country, then a uniform expanded genome profile would be beneficial for both law enforcement and testing laboratories.

If the sole purpose of an expanded genomic profile is to identify and apprehend a perpetrator, it would seem logical that the information derived from the test provide only descriptive information pertaining to physical features such as hair and eye color, height, weight/build and skin pigmentation. It would be preferable if these traits could be determined directly rather than inferred from ancestry due to the range of features in a given population (e.g., skin pigmentation in individuals with Indian ancestry) and admixture. Inclusion of behavioral or health information would be of much lesser importance unless it can be demonstrated to be useful in identification.

Since many genetic variants associated with physical traits are likely to be located in and around genes, and genes often have multiple functions, additional unintended information may be revealed. This poses a challenging dilemma to identify genetic variants for traits that do not reveal additional information pertaining to heath status. For example, it is commonly known that individuals with fair skin are at higher risk to melanoma given their increased sun sensitivity. In testing specimens for the red hair and fair skin genetic marker, additional information is revealed pertaining to the

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individual's risk of melanoma.[60] If such information is 'discovered', do the police or investigating authorities have an ethical obligation to share that information with the perpetrator, particularly if an intervention is available that could prevent disease onset or reduce risk of disease? Although it would seem obvious that an individual of fair skin would be at increased risk of skin cancer, perhaps a subset of fair skin individuals have a higher risk than others that would only be revealed through genetic analysis of the red hair/fair skin gene.

As science and technology moves closer toward the goal of being able to sequence the human genome for $1000 or less, it is foreseeable that many, if not all, individuals, will have their genome sequenced. If every individual has their genome sequenced as part of routine healthcare, the risk of discovery and need to disclose becomes less of an issue since the individual is already likely be aware of their health risk. However, the privacy of the information will still be of concern and it will be critical that the information is destroyed and no record is made in the individual's criminal record.[61]

Secondly, and perhaps more importantly, what is the added value of an expanded genome profile? Given that ancestry profiles or other genetic testing of physical or behavioral traits cannot provide an exact description, how will the added benefit of an expanded profile be determined? For a new medical innovation, a randomized clinical trial would be conducted to determine whether a new tool is better than current practice as measured by defined clinical outcomes. However, it is unlikely that a forensic trial could be performed since so many variables are either uncontrolled for or unknown. As mentioned earlier, comparison to statistics prior to the use of expanded genome profiling may be able to indicate the benefits of these new applications.

Given that the profile will be less than perfect, will it still be useful? A similar question has been asked regarding the use of race in medical decision-making: does knowing someone's race aid in diagnosis or treatment decisions? Some argue that while race is an imperfect surrogate for disease diagnosis or likelihood to respond to treatment, the information is nonetheless helpful.[62] Will defining race in forensics be more clear-cut than defining race for medical decision-making? In the absence of better identifying descriptors, having some data is better than no data at all. If the limitations of the test are not well understood (e.g., low predictive value), the test may potentially pose greater risks than no test at all due to false results, misinterpretation and wasted precious time in search of a perpetrator with an incorrect physical description.

One of the potential risks of testing are false positive and false negative test results. If an expanded genome profile indicates that the suspect is likely to be a white male with red hair and the police narrow their investigation to individuals matching this description, what are the consequences of this inaccurate description? Although it is probably not necessary for police investigators to understand the minute details of genome profiling, it is imperative that they understand the limitations of the test. Probability rather than certainty is the rule with genomics for complex traits and behaviors. At this early stage of testing where only one or a few genes are associated with a particular trait, we clearly have a long way to go before reaching a high

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confidence level of prediction of physical traits. Given the high stakes involved, a misinterpreted or unvalidated test potentially poses greater risks than no test at all.

When?

If time is selected as the major determining factor for when to use an expanded genome profile, what is the appropriate length of time before using this technology? For example, how long should investigators wait, if at all, to obtain an expanded genome profile – if the perpetrator is not apprehended within 24 hours, one week, or six months? Should it be influenced by the type of crime – a shorter wait period for rapes and homicides versus burglary and assaults? Although it may be presumed that immediate testing of the sample will provide investigators with valuable information to identify and apprehend the suspect, the questionable predictability of some results, cost, and potential risks may discourage the rush to profile.

The question of when to test would only arise if it were determined to be inappropriate or unfeasible to immediately test all crime scene specimens. Some type of triage approach may be useful to separate samples from crimes that may be tested at later dates from samples that would not be tested at all. This would also require a closer relationship between investigators and forensic services to ensure that testing commenced at the specified time. However, it would seem that the majority of risks of expanded genome profiling would be minimized if the genome profile only provides information on physical traits and all information including the sample is destroyed when no longer needed, thereby opening the way for automatic testing policy of all crime scene specimens without obvious suspects. If the need for some type of triage system is due to economic or technical reasons, the limited use of the expanded profile should be weighed against the benefits of testing all samples.

Where and How?

And lastly, and probably the largest issue of all, where will the information be stored and how will it be used? Since national DNA databases have been established for the storage of core DNA profiles from convicted and arrested individuals, the infrastructure to store an expanded genome profile is in place. However, for individuals who have been apprehended and photographs and/or a core DNA profile are stored in their record, an expanded profile has little additional use. Once an identity has been made, the information collected from an expanded profile would serve no additional purpose and should therefore be permanently destroyed.

How will the information be used? The obvious use of information gleaned from an expanded genome profile is to narrow the search to individuals meeting the description. In the case of the Louisiana serial rapist, police were misled by eyewitness accounts that the perpetrator was a white male.[63] However, DNA profiling indicated that the perpetrator was a black male and investigators re-focused their search based on the genetic description. While drag-netting based on geographic proximity to the crime (e.g., neighborhood or village) has raised criticisms of violations of civil liberties, the use of expanded genome profiling could also raise criticisms if the use and development of the profile is not confined to identification purposes.

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Will all jurisdictions be able to afford the costs of expanded genome profiles? Where will testing be performed? Comparable to new medical innovations that require cost-effectiveness or cost-benefit analyses, the value of added expenses allocated to expanded genome profiling needs to be demonstrated. However, if some jurisdictions, particularly small towns or rural communities, cannot afford the additional costs, will that place them at a significant disadvantage compared to more affluent communities? A report from the National Commission found huge disparities among resources of local law enforcement agencies.[64] Analogous to expansion of newborn screening programs with the advent of tandem mass spectrometry technology, law enforcement will bear the costs of new equipment, laboratory space, and training for personnel and tight budgets will be strained further. As an alterative, law enforcement agencies may outsource DNA profiling as is already done with newborn screening to reference laboratories to reduce in-house costs. However, given that many states are back-logged with samples awaiting the core DNA identification profile, the addition of expanded genome profiling will likely add to the ongoing burden.

Conclusion

As forensic profiling continues to rapidly move forward using genomic information to provide a 'genetic' sketch derived from biological crime scene specimens, the ethical issues associated with these new applications will continue to arise. While it is impossible to foresee every potential risk of these new technologies, it is prudent to address the known risks such as inaccurate (false positive) test results, individual and family privacy, and inflammation of racial profiling practices. It is essential that these issues be addressed concurrent to the development of forensic applications and not after their implementation.[65]

In my opinion, however, many of these issues can be addressed by clearly defining the use of expanded genome profiling for the sole purpose of gathering descriptive information of the perpetrator. As such, to the extent possible, genetic variants that do not provide useful information about the perpetrator's physical characteristics should not be included. Following capture and trial of the individual, the profile result would be removed from his/her record and replaced with the standard DNA profile. Under no circumstances, except for laboratory quality assurance and quality control purposes, will any research or analysis of samples or data be permitted. If adequate safeguards are developed to ensure only the intended use of the expanded genome profile, problems should be minimized.

At present, the science presents a much bigger challenge to the justifiable use of expanded genome profiling than the ethical and social issues. Given the uncertainties and lack of data regarding the predictive value of these tests, much more research is needed to understand the genetic mechanisms of the development of physical traits before such tests can be deemed useful and effective.

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