48. The Science and Business of Genetic Ancestry Testing

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At least two dozen companies now market "genetic ancestry tests" to help consumers reconstruct their family histories and determine the geographic origins of their ancestors. More than 460,000 people have purchased these tests over the past six years[1], and public interest is still skyrocketing.[2] Some scientists support this enterprise because it makes genetics accessible and relevant; others view it with indifference, seeing the tests as merely "recreational." However, both scientists and consumers should approach genetic ancestry testing with caution because (i) the tests can have a profound impact on individuals and communities, (ii) the assumptions and limitations of these tests make them less informative than many realize, and (iii) commercialization has led to misleading practices that reinforce misconceptions.

THE IMPACT OF "RECREATIONAL GENETICS"

Although genetic ancestry testing is often described as "recreational genetics," many consumers do not take these tests lightly. Each test costs a hundred to nine hundred dollars, and consumers often have deep personal reasons for purchasing these products. Many individuals hope to identify biological relatives, to validate genealogical records, and to fill in gaps in family histories. Others are searching for a connection to specific groups or places in Eurasia and Africa. This search for a "homeland" is particularly poignant for many African Americans, who hope to recapture a history

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stolen by slavery. Others seek a more nuanced picture of their genetic backgrounds than the black-and-white dichotomy that dominates US racial thinking.

Genetic ancestry testing also has serious consequences. Test-takers may reshape their personal identities, and they may suffer emotional distress if test results are unexpected or undesired.[3] Test-takers may also change how they report their race or ethnicity on governmental forms, college or job applications, and medical questionnaires.[4] This could make it more difficult to track the social experiences and effects of race and racism.[5] Genetic ancestry testing also affects broader communities: tests have led African Americans to visit and financially support specific African communities. Other Americans have taken the tests in hope of obtaining Native American tribal affiliation (and benefits like financial support, housing, education, health care, and affirmation of identity) or to challenge tribal membership decisions.[6]

LIMITATIONS

It is important to understand what these tests can and cannot determine. Most tests fall into two categories. Mitochondrial DNA (mtDNA) tests sequence the hypervariable region of the maternally inherited mitochondrial genome. Y-chromosome tests analyze short tandem repeats and/or single nucleotide polymorphisms (SNPs) in the paternally inherited Y chromosome. In both cases, the test-taker's haplotype (set of linked alleles) is determined and compared with haplotypes from other sampled individuals. These comparisons can identify related individuals who share a common maternal or paternal ancestor, as well as locations where the test-taker's haplotype is found today. However, each test examines less than 1 percent of the test-taker's DNA and sheds light on only one ancestor each generation.[7] A third type of test (DNAPrint's AncestryByDNA test) attempts to provide a better measure of overall ancestry by using 175 autosomal markers (inherited from both parents) to estimate an individual's "bio-geographical ancestry."

Although companies acknowledge that mtDNA and Y-chromosome tests provide no information about most of a test-taker's ancestors, more important limitations to all three types of genetic ancestry tests are often less obvious. For example, genetic ancestry testing can identify some of the groups and locations around the world where a test-taker's haplotype or autosomal markers are found, but it is unlikely to identify all of them. Such inferences depend on the samples in a company's database, and even

databases with 10,000 to 20,000 samples may fail to capture the full array of human genetic diversity in a particular population or region.

Another problem is that questionable scientific assumptions are sometimes made when companies report results of a genetic ancestry test. For instance, when an allele or haplotype is most common in one population,[8] companies often assume it to be diagnostic of that population. This can be problematic because high genetic diversity exists within populations and gene flow occurs between populations. Very few alleles are therefore diagnostic of membership in a specific population, but companies sometimes fail to mention that an allele could have been inherited from a population in which it is less common. Consequently, many consumers do not realize that the tests are probabilistic and can reach incorrect conclusions.

Consumers often purchase these tests to learn about their race or ethnicity, but there is no clear-cut connection between an individual's DNA and his or her racial or ethnic affiliation. Worldwide patterns of human genetic diversity are weakly correlated with racial and ethnic categories because both are partially correlated with geography.[9] Current understandings of race and ethnicity reflect more than genetic relatedness, though, having been defined in particular sociohistorical contexts (i.e., European and American colonialism). In addition, social relationships and life experiences have been as important as biological ancestry in shaping individual identity and group membership.

Many genetic ancestry tests also claim to tell consumers where their ancestral lineage originated and the social group to which their ancestors belonged. However, present-day patterns of residence are rarely identical to what existed in the past, and social groups have changed over time, in name and composition.[10] Databases of present-day samples may therefore provide false leads.

Finally, even though there is little evidence that four biologically discrete groups of humans ever existed,[11] the AncestryByDNA test creates the appearance of genetically distinct populations by relying on "ancestry informative markers" (AIMs). AIMs are SNPs or other markers that show relatively large (30% to 50%) frequency differences between population samples. The AncestryByDNA test examines AIMs selected to differentiate between four "parental" populations (Africans, Europeans, East Asians, and Native Americans). However, these AIMs are not found in all peoples who would be classed together as a given "parental" population. The AIMs that characterize "Africans," for example, were chosen on the basis of a sample of West Africans. Dark-skinned East Africans might be omitted from the AIMs reference panel of "Africans" because they exhibit different gene

variants.[12] Furthermore, some of the most "informative" AIMs involve loci that have undergone strong selection,[13] which makes it unclear whether these markers indicate shared ancestry or parallel selective pressures (such as similar environmental exposures in different geographic regions) or both.

The problems described here are likely responsible for the most paradoxical results of this test. For instance, the AncestryByDNA test suggests that most people from the Middle East, India, and the Mediterranean region of Europe have Native American ancestry.[14] Because no archaeological, genetic, or historical evidence supports this suggestion, the test probably considers some markers to be diagnostic of Native American ancestry when, in fact, they are not.

Thus, these tests should not be seen as determining the race or ethnicity of a test-taker. They cannot pinpoint the place of origin or social affiliation of even one ancestor with exact certainty. Although wider sampling and technological advancements may help,[15] many of the tests' problems will remain.

EFFECTS OF COMMERCIALIZATION

Although it is important for consumers to understand the limitations of genetic ancestry testing and the complex relation between DNA, race, and identity, these complexities are not always made clear. Web sites of many companies state that race is not genetically determined, but the tests nevertheless promote the popular understanding that race is rooted in one's DNA[16]—rather than being an artifact of sampling strategies, contrasting geographical extremes, and the imposition of qualitative boundaries on human variation. Because race has such profound social, political, and economic consequences, we should be wary of allowing the concept to be redefined in a way that obscures its historical roots and disconnects it from its cultural and socioeconomic context.

It is unlikely that companies (and the associated scientists) deliberately choose to mislead consumers or misrepresent science. However, market pressures can lead to conflicts of interest, and data may be interpreted differently when financial incentives exist. For scientists, these incentives include paid consultancies, patent rights, licensing agreements, stock options, direct stock grants, corporate board memberships, scientific advisory board memberships, media attention, lecture fees, and/or research support. Because scientific pronouncements carry immense weight in our society, claims must be carefully evaluated when scientists have a financial

stake in them. Unfortunately, peer review is difficult here, because most companies maintain proprietary databases.

As consumers realize that they have been sold a family history that may not be accurate, public attitudes toward genetic research could change. Support for molecular and anthropological genetics might decrease, and historically disadvantaged communities might increase their distrust of the scientific establishment.[17] These tests may also come up in medical settings: Many consumers are aware of the well-publicized association between ancestry and disease, and patients may ask doctors to take their ancestry tests into consideration when making medical decisions. Doctors should be cautious when considering such results.[18]

We must weigh the risks and benefits of genetic ancestry testing, and as we do so, the scientific community must break its silence and make clear the limitations and potential dangers. Just as the American Society of Human Genetics (ASHG) recently published a series of recommendations regarding direct-to-consumer genetic tests that make health-related claims,[19] we encourage ASHG and other professional genetic and anthropological associations to develop policy statements regarding genetic ancestry testing.

NOTES

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5. Ibid.
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7. A. Yang, *Chance* 20, 32–39 (2007).
8. K. Weiss and M. Fullerton, "Racing around, Getting Nowhere," *Evolutionary Anthropology* 14 (2005), 165,
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11. Weiss and Fullerton, op. cit.
12. S. Tishkoff et al., "Convergent Adaptation of Human Lactase Persistence in Africa and Europe," *Nature Genetics* 39 (2006), 31–40; A. Mourant, A. Kopec, and K. Domaniewska-Sobczak, *The Distribution of the Human Blood Groups and Other Polymorphisms* (London: Oxford University Press, 1976); M. Hamblin and A. Di Rienzo, "Detection of the Signature of Natural Selection in Humans: Evidence from

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14. AncestryByDNA, www.ancestrybydna.com/welcome/productsandservices/ancestrybydna/ethnicities.

15. M. Shriver and R. Kittles, *Nature Reviews Genetics* 5 (2004), 611.

16. DNAPrint, Frequently Asked Questions, no. 1, www.ancestrybydna.com/welcome/faq/#q1.

17. J. Reardon, *Race to the Finish: Identity and Governance in an Age of Genomics* (Princeton, NJ: Princeton University Press, 2004).

18. In contexts such as gene mapping and genome-wide associations, genetic ancestry information can protect against confounding by population stratification or provide evidence of the population origin of specific susceptibility alleles. See M. Enoch et al., "Using Ancestry-Informative Markers to Define Populations and Detect Population Stratification," *Journal of Psychopharmacology* 20 (2006), 19. These applications are much narrower than determination of individual ancestry.

19. K. Hudson et al., "ASHG Statement on Direct-to-Consumer Genetic Testing in the United States," *American Journal of Human Genetics* 81 (2007), 635.