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Genetic exceptionalism. Too much of a good thing?

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The current issue of *Genetics in Medicine* features a commentary that explores how genetic information might be treated in the (increasingly electronic) medical record.[1] The authors, all members of the Personalized Health Care Work Group of the American Health Information Community (AHIC), propose special protections for genetic information within the electronic medical record. Their conclusions are in keeping with a long tradition of genetic exceptionalism in our specialty. Applying this concept to the medical record, however, would seem to create barriers to genetically informed health care. Is it time to abandon genetic exceptionalism?

A consideration of different types of genetic information suggests that genetic exceptionalism is more likely to be advocated—and potentially desirable—in inverse relation to its clinical utility. Nobody would wish to sequester a diagnosis of phenylketonuria, because it is actionable information, essential to assuring the infant a healthy future. The value of newborn screening hinges precisely on rapid dissemination of the results, so that appropriate treatment can be provided. On the other hand, a diagnosis of Huntington disease (HD) might result in stigma and discrimination, in large part because there is no specific or curative therapy. Calls for limiting access to this information, in a fashion similar to records about mental illness, might be reasonable, (though in fact HD results are not usually treated this way). And in the hoped-for future, when effective therapies are developed to prevent or treat HD, barriers to the dissemination of that information would be inappropriate. Thus, as genetic information increasingly becomes medically useful, it challenges the concept of genetic exceptionalism.

At the core of the call by McGuire et al.[1] (this issue, page 495) for special protection of genetic information in the medical record is the recognition that genetic information is unique, and thus is a powerful identifier. DNA is also immutable (allowing for the nontrivial exception of somatic mutations). But these legitimate claims do not provide a justification for special treatment of genetic information. The rest of the medical record is highly "identifying" in its own right, and many nongenetic diagnoses are immutable—for example, the diagnosis of multiple sclerosis or Alzheimer Disease. As these examples illustrate, the medical record contains much sensitive nongenetic information: in fact, we anticipate that most people would feel more comfortable sharing their CYP2C9 alleles with a third party than their social security number, previous hospitalizations, or history of testing for sexually transmitted diseases, all information likely to be found in the medical record. The purpose of the medical record is to provide specific and detailed medical information about a particular individual; by its nature it contains highly personal information. Americans' strong interest in maintaining medical privacy has spawned the Health Insurance Portability and Accountability Act Privacy Law—overkill in the eyes of some, but evidence of an appropriate commitment to robust protection of the entire medical record.

Genetics is, of course, not only an individual identifier but also a predictor of future disease risks and drug response. Such genetic prediction is often cited as another justification for genetic exceptionalism, and the AHIC statement by McGuire et al.[1] is motivated in part by the expectation that an increasing number of genetic tests will be used as predictors. This position implies that genetic risk prediction is qualitatively different from other medical risks—but to the extent that a distinction is valid, it is arguably the case only for (mostly rare) highly penetrant genotypes. As geneticists well understand, the predictive power of gene variants associated with common complex diseases is limited, because genetic risk is only one of many contributors to disease. And while genomics applies a new technology to risk prediction, it does not necessarily provide information that is inherently different from the other predictors commonly used in health care, such as age, gender, blood pressure, smoking status, cholesterol level, or family history. The fact that the risk derives from a DNA-based test does not provide an obvious rationale for setting it apart in the policy arena. Rather, the more clinically useful the test, the more it should be readily accessible to health care providers.

The family implications of genetic risk information also provide limited justification for genetic exceptionalism in our view. Again, penetrance of the genotype may be a more important factor in policy deliberations than the use of genetic technology to generate results. The diagnosis of neurofibromatosis, typically done by physical examination, has dramatic health implications for family members; whereas the identification of a gene variant associated with a modestly increased risk of diabetes or heart disease will have little significance for the health care of relatives. And indeed, if the day comes when effective interventions exist for low penetrance gene variants; the impetus will be to test widely, independent of family history. In the case of the highly penetrant condition, a potential duty to inform family members is sometimes claimed.[2] Ironically, this

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example of genetic exceptionalism leads to consideration of limited breaches of medical confidentiality rather than to a call for sequestering the information more securely within the medical record. However, neither duty to warn nor the need for special protection can be argued persuasively for genetic risk factors emerging from current research.

A further challenge to genetic exceptionalism is that the "genetic information" to be protected cannot be readily or neatly defined. Is characterization of tumor DNA a genetic test? Or should the definition be limited to tests for inherited characteristics? We can infer significant aspects of an individual's genotype from such measurements as hemoglobin electrophoresis and serum metabolites, and physical examination is a more reliable method than a DNA-based test for many genetic disorders. Yet we do not see calls for sequestering exam findings of café au lait spots or tendinous xanthomas within the medical record. The very difficulty of defining "genetic" information should give us pause with regard to treating the results of "genetic tests" differently from other clinical findings in the medical record.

In considering genetic exceptionalism, it is important not to conflate issues germane to clinical care with those that are unique to research. If we accept that the confidentiality of medical records should be aggressively protected, the concerns outlined by McGuire et al.[1] are more relevant to genomic research than to the clinical medical record, particularly in an era when large biorepositories are being created with the expectation of widespread sharing of data among researchers. Effective genomic research requires clinical data and sequence information. The AHIC statement indicates the need for caution, and careful attention to informed consent procedures and research oversight when genomic researchers seek access to medical records.

If our field of medical genetics realizes the bright future, often predicted for it, genetic and genomic information will increasingly aid medical decision-making in many clinical arenas. This promise calls into question—in our view appropriately—a core assumption of our field: that genetic information is qualitatively different from other types of medical information and thus must be treated in a different way. Genetic information has historically had little impact on health outcome, because it has been used primarily to diagnose conditions for which treatment was limited or lacking. This bleak history has provided a justification for genetic exceptionalism. But we can look optimistically to a different future. Not only can we expect progress in the development of treatments for rare genetic diseases, we can also look to the productive use of genetic risk factors in drug treatment, classification of heterogeneous diseases, and prevention. In this future, genetic exceptionalism is a questionable guide to organization of the medical record. The more genetic information can be used to promote health, the more accessible the information should be to clinicians.

Finally, it seems that much of the discussion about genetic exceptionalism often misses the primary point. If we are correct in our preceding arguments about how little genetic information differs from other types of medical data, why is it that this debate has such strong "legs"? Why do all of us undeniably have at least a nagging sympathy with the idea of genetic exceptionalism? We would argue that there are two reasons: the first is that genetics is at the heart of our most profound relationships: DNA testing can confirm or deny parenthood and shed light on our ancestry. The second derives from a cultural belief that genetics largely determines who we are (despite many observations to the contrary).[3] This belief takes on special power in considering the genetic contributors to personality and behavior.[4] As with other complex traits, genotype is one among many etiological factors, and the study of behavioral genetics poses difficult methodological problems. Despite these limitations, it is clear that genetic variation is a factor in human behaviors. It follows that gene variants associated with problematic behaviors could become a source of stigma; even if the associations are weak. Accordingly, if there is a role for the special treatment of genetic information, it may apply to those aspects of our genome that bear on personality traits, antisocial behaviors, and psychiatric disease. There is ample precedent in medicine for the special treatment of psychiatric information, and policies related to genetic information should be informed by this experience.

All of our medical information is precious, private and deserves vigorous protection. The trick is to provide such protection while also ensuring that legitimate medical providers have quick and reliable access to it. Instead of parsing our information by type as "genetic" or "nongenetic," we must advocate for a sensible and just health care system that protects against the inappropriate use of our medical information as a whole and ensures that all have access to the fruits of the tremendous advances that we are witnessing in modern medicine, genetic or otherwise.

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