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**GTR RFI Comments**

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We roundly applaud the idea of a Genetic Testing Registry (GTR). To have a centralized, trusted resource that can provide stakeholders--especially patients--with reliable information regarding genetic tests' validity and utility will be invaluable. We suspect that a modest investment in such a registry will pay for itself many times over in improved patient access and care.

That said, we are not sure that clinical validity and utility will ultimately prove to be the most useful aspects of a GTR. In collecting information on the effect of intellectual property on access to genetic testing for Long QT syndrome (LQTS) at the behest of the Secretary's Advisory Committee on Genetics, Health and Society, we and our colleagues in the Duke Center for Public Genomics (supported by grant P50 HG003391 from the National Human Genome Research Institute) canvassed patient members of the C.A.R.E. Cardiac Arrhythmias Support Community, and those suffering from neurological conditions (e.g., support groups for genetic disorders causing cerebellar ataxia) and cancer. Again and again they worried about cost and insurance coverage in addition to their actual clinical results.

Some such concerns have been ameliorated by the Genetic Information Nondiscrimination Act, but many have not (e.g., risk evaluation for Alzheimer's disease and long-term care insurance). Many people were not aware of their testing alternatives, either from other commercial labs or university labs. Very few knew about business arrangements, costs, or even opportunities to get help seeking coverage and reimbursement for tests that could alter the course of their lives. Therefore, in the interest of transparency, we urge NIH to include pricing and insurance coverage information in the GTR, or at least linkages to resources that clinicians and patients can use to find out information about the tests they might use. Since these parameters often change, obviously it would be crucial for the GTR not to be a static database that can only be updated at infrequent intervals or by negotiating an onerous bureaucracy.

As for utility, we believe frank discussion of the limits of genetic testing is just as important as information about access, not only for personal genome scans but for monogenic and oligogenic disorders as well. A database should mention and/or link to verifiable data about the uncertainties and probabilistic inferences associated with genetic testing for any given disorder. If we were at risk or caring for persons at risk for LQTS or hereditary breast cancer, for example, we would want to know what fraction of results are classified as so-called "variants of unknown significance (VUS)," how those are dealt with by the clinical laboratory and referring clinician, how they are communicated to the patient and her caregivers, and what options are available to a patient with a VUS.

Additionally, the reporting of clinical data correlated to genotype has recently come to our attention. In cases where the testing laboratory is a sole provider or one of just a few facilities offering a test (e.g., due to exclusive patent rights or for other reasons), it is essential that data relevant to interpretation of genotype-phenotype correlations be publicly shared. Otherwise, clinical data will be held as proprietary assets, collected disease-by-disease by individual testing laboratories and thus unavailable to health professionals or patients who need the information to interpret test results. Myriad Genetics, for example,

was far-sighted in being the largest contributor to the Breast Cancer Information Core for years, but ceased contributing data in 2004, so genotypes that have been characterized as variants of unknown significance since that time are held by the company as a proprietary asset. This is good for Myriad as a business asset, and perhaps the company should get a financial reward for generating this information if it agrees to share the data, but it is clear that in the long-run, such atomized and proprietary data storage is antithetical to interpretation of genotype data in an era of genome-wide analysis. The Registry might consider setting conditions of participation or other measures to ensure that genotype-phenotype data are collected in a way that ensures clinical translation and scientific advance.

Finally, in its report to SACGHS, the Duke Center for Public Genomics found an alarming lack of transparency among holders of gene patents, which, in some cases, has led to misunderstandings, intimidation, and de facto monopolies. Some companies do not even list their licensed patents, and almost none indicate what uses are exclusively or not exclusively licensed (and thus available for others to use or license). The recent decision invalidating some of the Myriad Genetics breast cancer gene patents notwithstanding, a GTR is an opportunity for transparency not only with respect to clinical, pricing and insurance data, but intellectual property as well. The law in this area is in flux and will be uncertain for a few years, but the need to know what intellectual property exists, who owns it, and how it is being used and made available is essential for understanding and working in the world of genetic testing, and absence of this information, or at least links to it, will make the registry far less useful than it might otherwise be. Most such information is not subject to changes in legal interpretation, but matters of fact and documentation. Given that the vast majority of intellectual property pertinent to genetic testing results from federal or nonprofit funding, this lack of transparency is particularly galling, and should be a major concern for NIH itself.

It seems to us that it would be well worthwhile to include space in the GTR asking what patents genetic test providers hold or have licensed, in what jurisdictions, how they have been enforced against whom, and whether there are opportunities for sub-licensing, etc. Perhaps we are naive, but we would like to think that inclusion of this information could set a new, more open precedent in commercial molecular diagnostics and personalized medicine, reduce costly litigation, help clear the path for wider availability of genetic tests, and benefit patients and their families as well as the businesses whose success will entail multi-allele and/or full-genome analyses.

Thank you for your consideration.

Sincerely,

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