

Response to GTR Request for Comments

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General Comments:

A centralized repository of information about genetic tests offered for clinical diagnostic purposes could be enormously useful to researchers, clinicians, clinical genetics laboratory directors, manufacturers and patients. A voluntary, community effort to develop standards for determining clinical utility, analytical and clinical validity, and the most effective methods for test interpretation and reporting, will be extremely valuable. This is particularly true as we move towards whole genome or whole exome analysis of individual patients for whom interpretation of pathogenic vs. benign variants and the resolution of “variants of uncertain clinical significance or VOUS” becomes an increasingly daunting challenge.

To maximize the utility of the GTR, I would suggest the proposal go beyond the current “repository of information about genetic tests” to also include a “repository of genetic test results”. There are several good pilot projects and model systems for large-scale data sharing of genetic test results that could be utilized in developing similar models for GTR. These include the CETT (Collaboration Education and Test Translation) pilot program developed by the Office of Rare Disease Research (ORDR/NIH)(see <http://rarediseases.info.nih.gov/cettprogram/default.aspx>), the ISCA (International Standards for Cytogenomic Arrays) Consortium hosted at Emory (<https://isca.genetics.emory.edu/>), and the MS/MS Data Project hosted by the Mayo Clinic as part of HRSA’s Newborn screening and genetics regional collaboratives (http://region4genetics.org/msms_data_project/data_project_home.aspx). All three of these projects recognize that many genetic diseases are individually rare, and so data sharing across many different laboratories allows a more rapid accumulation of empiric data that can be mined and analyzed to extract new knowledge that will improve the quality of future genetic testing. The ISCA Consortium project has the specific goal of making data submission of clinical genetic laboratory data as seamless as possible-essentially a single click of a “submit to NCBI” button that will de-identify patient data (genotype and phenotype) and reformat the data for electronic submission to dbGaP and dbVar databases. This model may be extended in the future to capture phenotypic data directly and automatically from electronic medical records (EMRs) to be paired with the genetic test data from clinical laboratories.

Although GeneTests has been an extraordinarily important resource for all clinical geneticists and genetic counselors on a daily basis, it has had a very restricted role as a simple “directory” of genetic testing. Given the rapidly growing pace and volume of genetic data being generated during the routine course of patient care using more powerful genetic tests, the time is ripe for a very creative expansion of our goals of optimizing and leveraging the opportunities to improve genetic test quality and access, and realizing the potential value of large, shared databases for new knowledge generation and improved clinical decision-making related to genetic test results.