Reference and quality control (QC) materials are essential for many aspects of genetic testing. These materials, which are tested alongside patient samples, allow the laboratories to detect errors due to test system failure or operator error. In addition, reference materials are needed for test development and validation, lot-testing of new reagent batches and for proficiency testing/external quality assessment programs (PT/EQA).

Over 2400 genetic tests are currently offered in clinical laboratories, however, for the vast majority of these tests, no publicly available characterized reference or QC materials are available. In the absence of these publicly available materials, laboratories must improvise to obtain these reagents and, in some cases, develop and run assays without adequate controls. Often, DNA derived from left over patient specimens, which is not easily available or renewable, is used as a reference material. Laboratories also utilize synthetic DNA or DNA isolated from cell lines. All of these materials must be validated by the laboratory prior to use as QC or reference materials.

The Centers for Disease Control and Prevention (CDC) has been involved since 1995 in efforts to develop appropriate and well characterized reference materials for use by the genetics community. In 2004, the Genetic Testing Reference Materials Coordination Program (GeT-RM) was established at the CDC in partnership with the genetics community. The goal of this program is to coordinate a self-sustaining community process to improve the availability of characterized genomic DNA materials for quality control, proficiency testing, test development/validation and research. The GeT-RM also facilitates information exchange between users and providers of reference materials. Although the GeT-RM Program is coordinated by the CDC, all of the actual work, including decisions about reference material priorities, specimen collection, material development and characterization occurs through voluntary collaborations with laboratories in the genetics community. Cell lines with confirmed genotypes are considered the preferred type of control for DNA based genetic testing as they most closely resemble an actual patient specimen. Thus, the GeT-RM’s efforts focus on this material type.

The GeT-RM program has characterized more than 400 cell line based genomic DNA reference materials for a number of genetic disorders, including: fragile X, disorders on the Ashkenazi Jewish Panel (Bloom syndrome, Canavan disease, Fanconi anemia, familial dysautonomia, Gaucher disease, mucolipidosis IV, Neimann Pick disease and Tay Sachs disease), cystic fibrosis, Huntington disease, MTHFR-related homocysteinemia, alpha1-antitrypsin deficiency, multiple endocrine neoplasia, BRCA1 and BCRA2-related cancers, Duchenne muscular dystrophy, myotonic dystrophy, Rett syndrome, and a large-scale study of DNA from107 cell lines for a number of polymorphisms in 20 pharmacogenetic loci. Each of these genomic DNA materials was tested in between 3 and 10 clinical genetic laboratories using a variety of genetic assays, including DNA sequence analysis. These materials are publicly available from the Coriell Cell Repositories. We have recently started projects to develop reference materials for whole genome sequencing, molecular cytogenetics, molecular oncology, 231 pharmacogenetic loci and HLA.

To date, the GeT-RM has focused its efforts on DNA based testing for inherited genetic disorders. However, there is a similar lack of reference materials for other areas of genetics, including molecular oncology, molecular infectious disease testing and biochemical genetic testing. Mechanisms to address reference material needs for these areas are also being considered.

The GeT-RM website (http://www.cdc.gov/dls/genetics/rmmaterials/default.aspx) provides a comprehensive source of molecular genetic reference material information to the genetic testing community. The website is grouped into three subject areas; inherited genetic diseases and pharmacogenetics, molecular oncology and infectious disease. Information about available reference materials, including applicable characterization studies and results are provided. The website also features comprehensive searchable databases of commercially available reference materials for both molecular oncology and infectious disease and general information about reference materials, including pertinent research articles, a list of reference material sources (manufacturers, repositories, etc.), a list of relevant guidance and oversight websites and documents.
GeT-RM Publications:


