



Ensuring the Quality of Genetic Testing

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How does the genetic testing laboratory know that a test is working properly and will give accurate results?





Quality Control



Reference or Quality Control (QC) materials are used to:

- Assess whether the genetic test is working properly and can detect genetic alterations (mutations)



What is the Ideal Reference Material for Genetic Testing?

(Ideally) Blood from patients with characterized mutations or alleles known to cause the disorder

- (Practically) Material that closely resembles a patient sample so it can be used to monitor and evaluate all steps of the testing process
 - Could be a cell line or purified DNA
 - Studied extensively and proven to contain particular mutations(s) (alleles)

Reference materials are also important for:

- Comparison of results between laboratories
- Proficiency testing samples
- Test calibration
- Development of new genetic tests
- Validation of new genetic tests

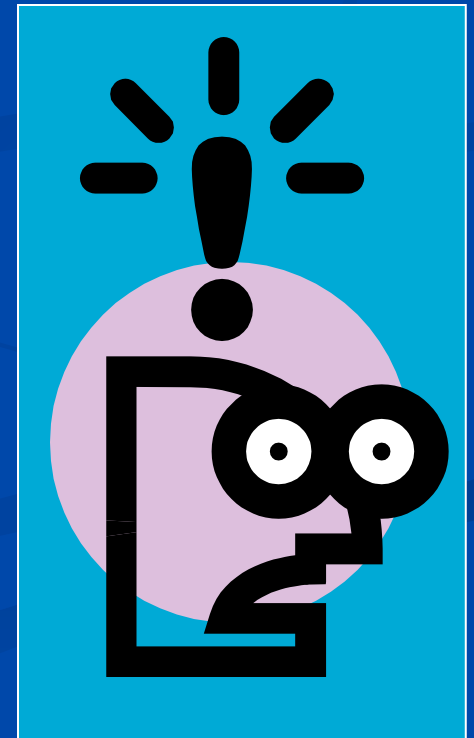
Reference Materials for Genetic Testing

- Genetic testing volume is increasing
- Many new tests are being introduced

However.....

Positive controls samples are **NOT** publicly available for most genetic tests!

(and even fewer have been verified)





Example - Cystic Fibrosis (CF) Genetic Testing

Collected information about 35 US testing labs

- All clinical labs tested for at least the ACMG recommended 23 CF alleles
- Identified 102 different CF alleles tested in US clinical labs
 - There are cell lines for only 42 alleles

 **60 alleles not available as cell lines !**

Other Examples

Fragile X and Huntington Disease

- Genetic tests where the size of the gene is measured
- **VERY** technically difficult tests
- Precise size measurement is needed for proper diagnosis

Few characterized reference materials available!



When No Reference Materials are Available.....

- Labs use previously assayed patient samples
 - **Problem**-how do you know that they were assayed correctly if the lab lacks controls?
- Synthetic controls are available for a few tests
 - **Problem**- synthetic DNA may not perform the same as human DNA in the assay
- Sometimes labs run assays without adequate controls
 - **Problem**- not ideal, may increase chance of errors!



Genetic Testing Reference Material Program (GeT-RM)

A CDC-based program to improve the availability of reference materials for genetic testing

Collaboration with genetic testing community

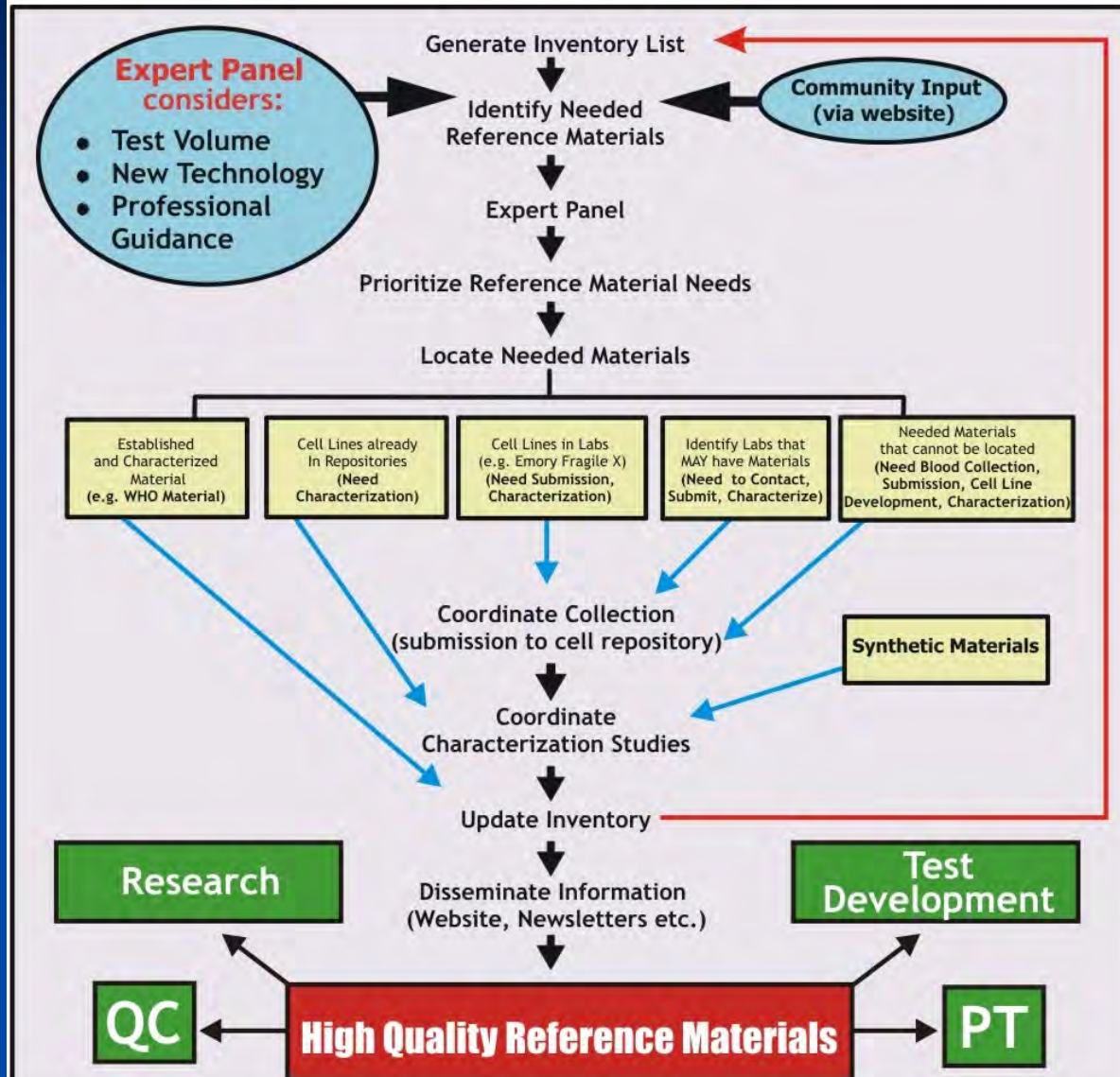
- Academic and clinical genetic testing labs
- Government agencies
- Cell repositories
- Industry
- Professional organizations



Roles of GeT-RM

- Improve and coordinate information exchange about reference materials
- Monitor reference material needs of genetic testing community
- Facilitate submission, development and characterization of reference materials
- Develop a sustainable community process for continued reference material development

GeT-RM Flow Chart





GeT-RM Website

<http://wwwn.cdc.gov/dls/genetics/qcmaterials/default.aspx>

■ Provides information about:

- Availability and validation status of a variety of reference materials
- Reference material needs
- How to contribute potential reference materials
- Professional and regulatory guidance
- References
- CDC's efforts to improve the quality of genetic testing

■ Solicits input from the genetic testing community



Coriell Institute for Medical Research

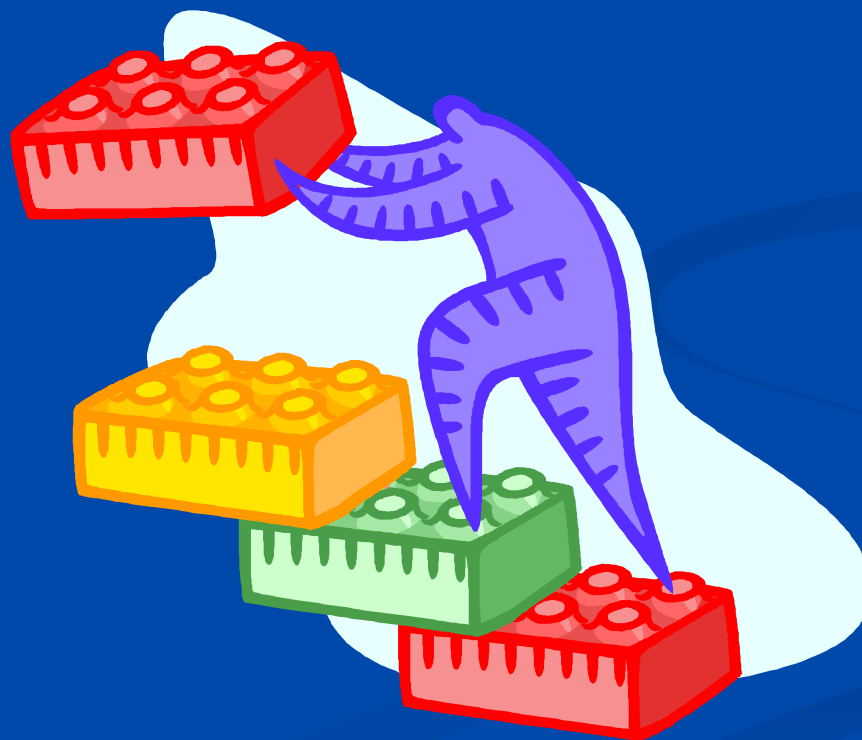
<http://ccr.coriell.org/Default.aspx>

National Institute of General Medical Sciences (NIGMS) Human Genetic Cell Repository

<http://ccr.coriell.org/Sections/Collections/NIGMS/?SsId=8>

- Non Profit -Supported by NIH
- Coriell distributes DNA and cell line samples to facilitate genetic research and improve laboratory quality since 1972

GeT-RM Reference Material Development Projects





Ashkenazi Jewish Panel



Recently completed characterization of 27 cell lines from Coriell as reference materials for genetic testing of 9 disorders common in the Ashkenazi Jewish population

- Tay-sachs disease
- Canavan disease
- Glycogen storage disease type 1a
- Familial dysautonomia
- Mucopolysaccharidosis type IV
- Niemann-Pick disease type A
- Fanconi anemia group C
- Bloom syndrome
- Gaucher disease



Huntington disease and Fragile X

The GeT-RM has completed
characterization of:

- 14 Huntington cell lines from Coriell
- 21 fragile X cell lines from Coriell

For use as reference materials!



GeT-RM Current and Future Reference Material Development Projects

- Cystic fibrosis
- Breast Cancer
- Newborn Screening disorders
- Others???



Continued Reference Material Development...

Big Problem...

Lack of available cell lines!!!!!!





Development of New Reference Materials

2 Methods

1. Establish new cell lines
2. Identify mutations in existing cell lines

Problem-

Limited access to patient blood samples!



GeT-RM is expanding into other areas of molecular testing -

- ✓ Molecular Oncology
- ✓ Infectious Disease
- ✓ Biochemical Genetic Tests



THANK YOU



GeT-RM:

<http://wwwn.cdc.gov/dls/genetics/qcmaterials/default.aspx>