State of the Art and Current Projects

ICORD 2008

Roberta A. Pagon, MD
Principal Investigator, GeneTests
Professor, Pediatrics
University of Washington, Seattle

www.genetests.org

Information resource for healthcare providers to help integrate genetic services into patient care

Located at
University of Washington
Seattle, WA

Funded by
National Institutes of Health

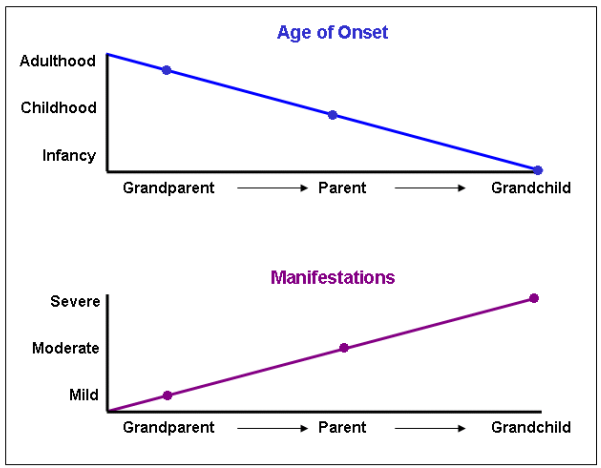
- ***GeneReviews*:** "User manual" for genetic testing for specific diseases
  - >430 *GeneReviews*
  - One new Review added each week
- **Laboratory Directory:** "Yellow Pages" of genetics labs
  - ~ 610 Clinical and research laboratories
  - ~1550 Inherited diseases
- **Clinic D** ·290 res s" of g
- **Illustrat** :ounse

anticipation: The tendency in certain genetic disorders for individuals in successive generations to present at an earlier age and/or with more severe manifestations; often observed in disorders resulting from the expression of a **trinucleotide repeat mutation** that tends to increase in size and have a more significant effect when passed from one generation to the next

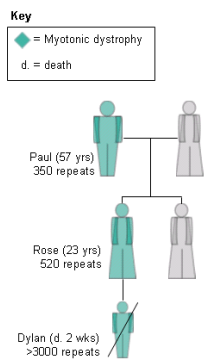
Case Example (anticipation): Myotonic dystrophy

Paul is a 57-year-old man with myotonic dystrophy, a neuromuscular disorder caused by a trinucleotide repeat mutation inherited in an autosomal dominant manner. Paul noticed muscle weakness in his late 20s and now has difficulty opening jars and climbing stairs. His 23-year-old daughter, Rose, experienced onset of muscle cramping and weakness as a teenager. Her son, Dylan, born after a pregnancy complicated by polyhydramnios and poor fetal movement, was extremely hypotonic and expired at two weeks of age of respiratory failure. Trinucleotide repeat analysis of the *DMPK* gene reveals that Paul has 350 CTG repeats, Rose has 520 repeats and Dylan over 3000 repeats, consistent with the observed increase in severity of the disorder in subsequent generations.

Learn More



Case Example



	DMPK gene CTG Repeats	Onset	Clinical Findings
Paul	350	3rd decade	Myotonia, weak facial muscles, general muscle weakness
Rose	520	2nd decade	Myotonia, weak facial muscles, general muscle weakness
Dylan	>3000	Prenatal	Severe weakness, respiratory failure

GENETests

Testing for Inherited Disorders From the Clinician's Perspective

- Molecular genetic testing
- Biochemical genetic testing
- Specialized cytogenetic testing (e.g., FISH, chromosomal breakage studies)

Current Projects

- Hosting by NCBI
- Standard Mutation Nomenclature
- Collaboration with EuroGentest
- Representation of New Tests

GENETests

Hosting by NCBI

- *GeneReviews* published on Bookshelf
- GeneTests Laboratory Directory
  - –Integrates search results with OMIM, PubMed, GHR, EntrezGene, etc
  - –Allows GeneTests staff to focus on content, not technical issues

Standard Mutation Nomenclature

Use of standard mutation nomenclature with reference sequence enables data sharing with mutation databases

Standard Mutation Nomenclature[1]

[Gene Symbol] Allelic Variants Discussed in this *GeneReview*

Class of Variant Allele	DNA Nucleotide Change (Aliases [2])	Protein Amino Acid Change	Reference Sequence [3]
Normal			
Pathologic			

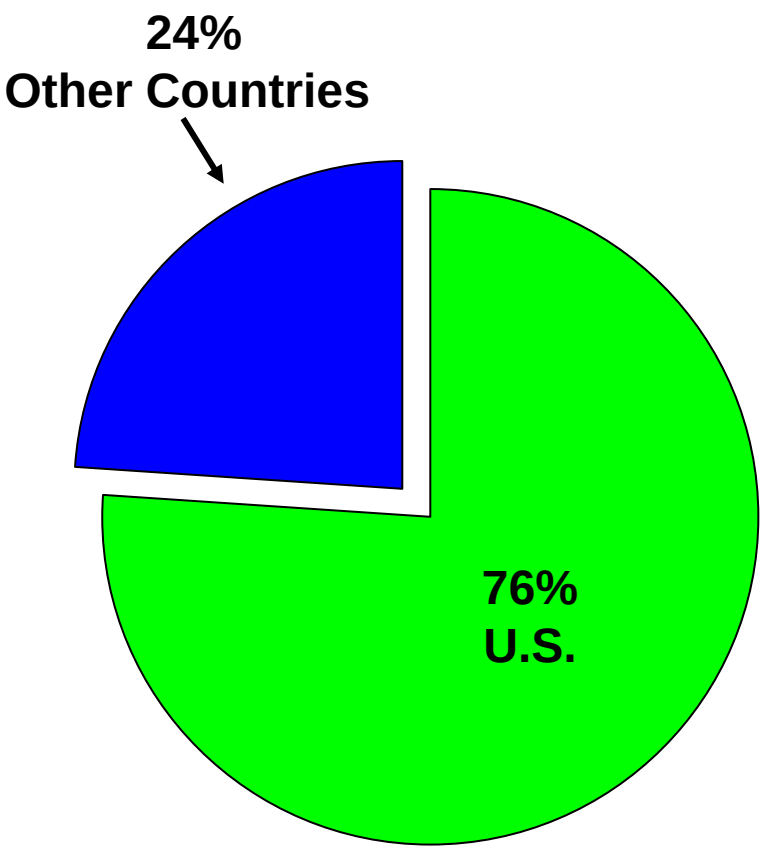
[1]per Human Genome Variation Society (www.hgvs.org).
[2]Variant designations that do not conform to current naming conventions
[3]Reference sequence (www.ncbi.nlm.nih.gov/Genbank/index.html)

Collaboration with EuroGentest

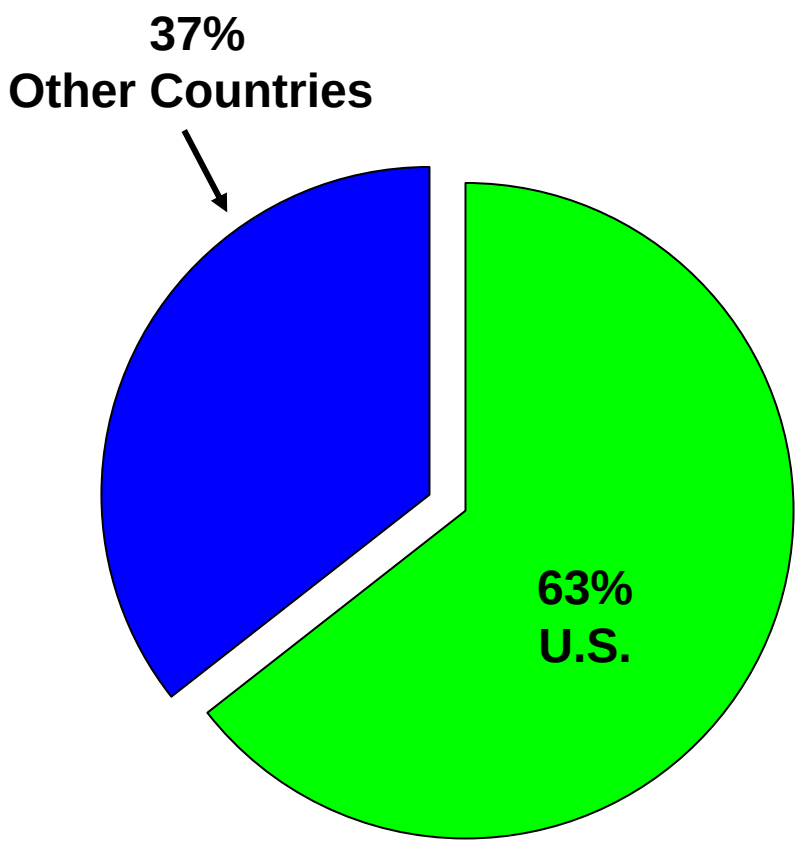
GENETests

Laboratories

2001 (N = 498)



2007 (N = 616)



Collaboration

- **GeneTests:** Display information about testing for inherited diseases provided by clinical laboratories listed in EuroGentest
- **EuroGentest:** Display information about testing for inherited diseases provided by clinical laboratories in the US and Canada listed in GeneTests

Collaboration Benefits to GT/EGT Users and Labs

- Users: Improved access to worldwide information on clinical testing for rare inherited diseases
- Labs: Broader market for rare disease testing

GENETests

Representation of New Tests: "Disease Panels"

Testing multiple genes by phenotype

- X-linked mental retardation
- Deafness
- Ataxia

GENETests Staff

Principal Investigator Roberta A Pagon, MD

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