Genetics, The Duchenne Registry And Your Family

Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

Kayla Quirin, MS, CGC

Certified Genetic Counselor

Topics for Today:

1. Dystrophinopathy 101
2. Genetics and the importance of genetic testing
3. Connecting to research through The Duchenne Registry
4. Answer your questions!

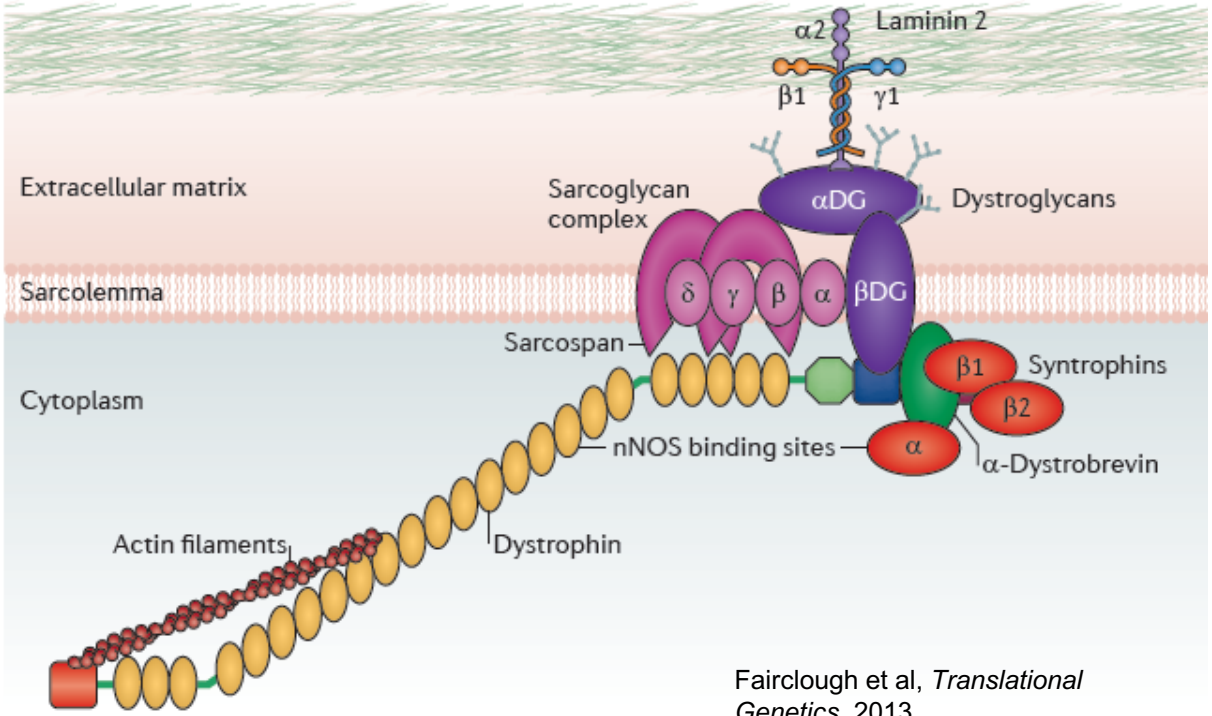
What is Duchenne?

Duchenne and Becker muscular dystrophies are genetic conditions caused by changes in the gene that makes dystrophin (DMD). As a result, dystrophin is not made or is made incorrectly. Without dystrophin, muscles are not able to function or repair themselves properly.

Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

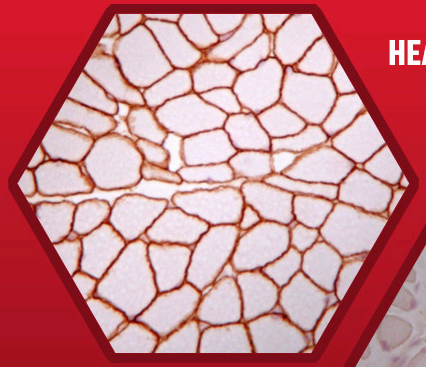
Duchenne and Becker are dystrophinopathies



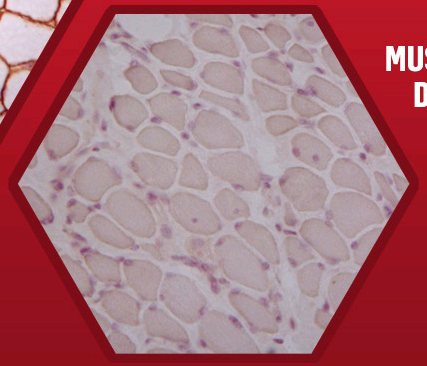
Fairclough et al, *Translational Genetics*, 2013

DUCHENNE'S EFFECT ON MUSCLES

Without dystrophin, muscle cells are damaged, and, over time, are replaced with scar tissue and fat in a process called fibrosis.



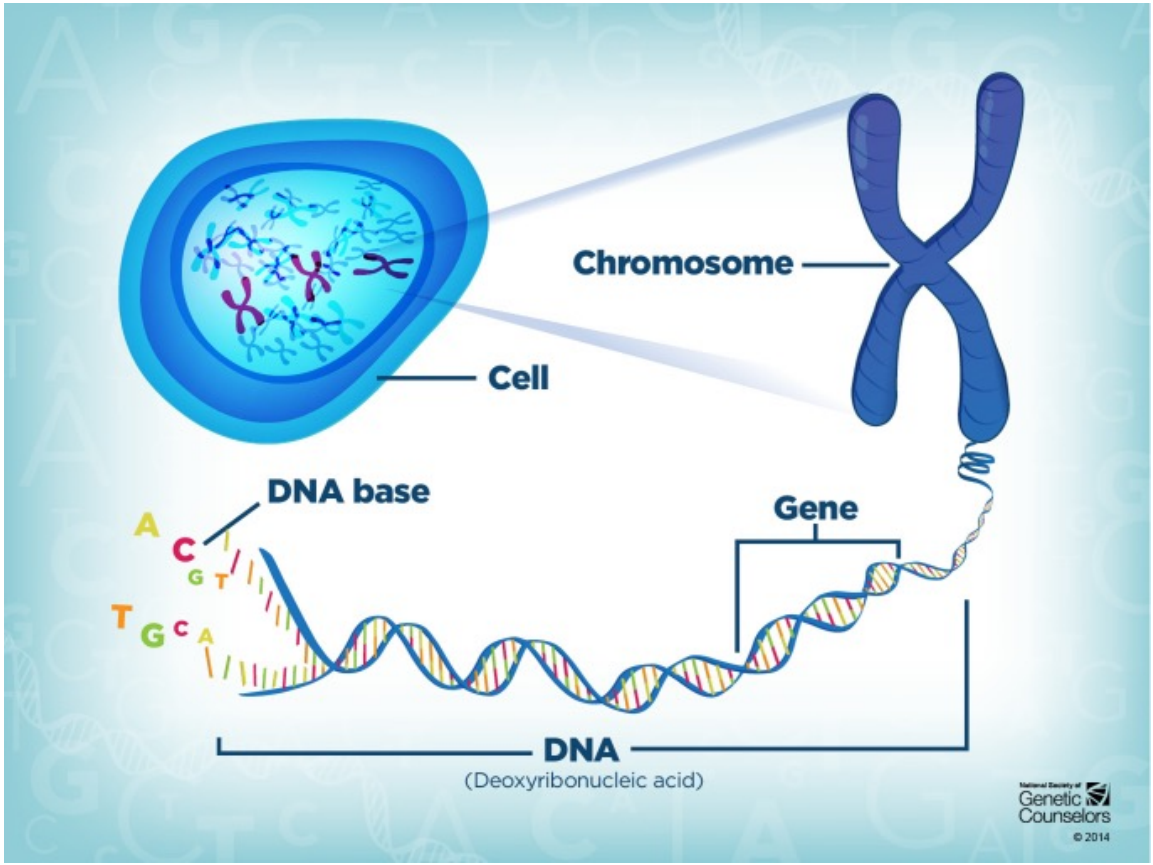
HEALTHY MUSCLE TISSUE



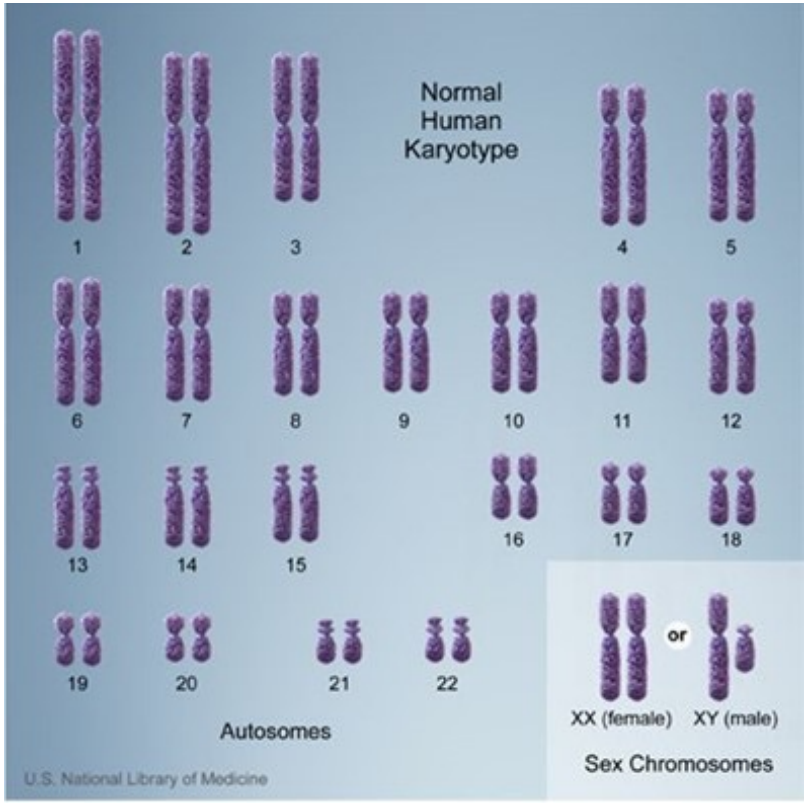
MUSCLE TISSUE WITH DUCHENNE MUSCULAR DYSTROPHY


DUCHENNE IS NOT JUST A DISEASE OF THE MUSCLES.
IT AFFECTS EVERY SYSTEM IN THE HUMAN BODY.
DUCHENNE101
MUSCLE
BONE
HEART
LUNG
DIGESTION
BEHAVIOR
GROWTH

Genetics Review

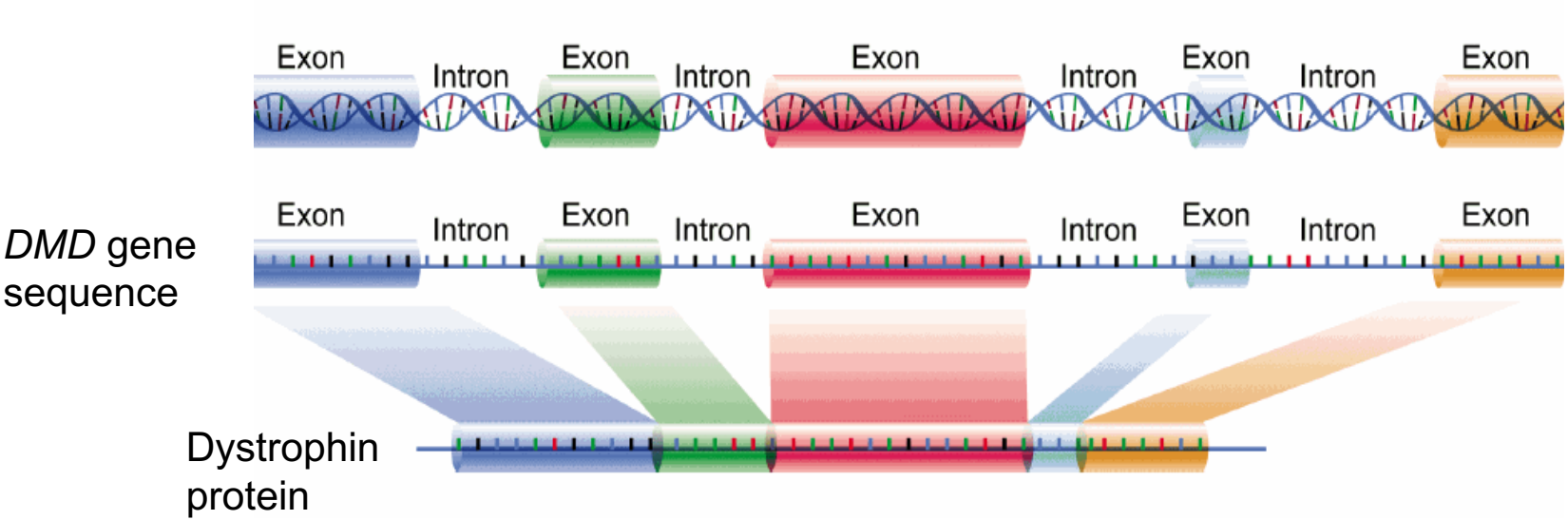


Typical Human Karyotype

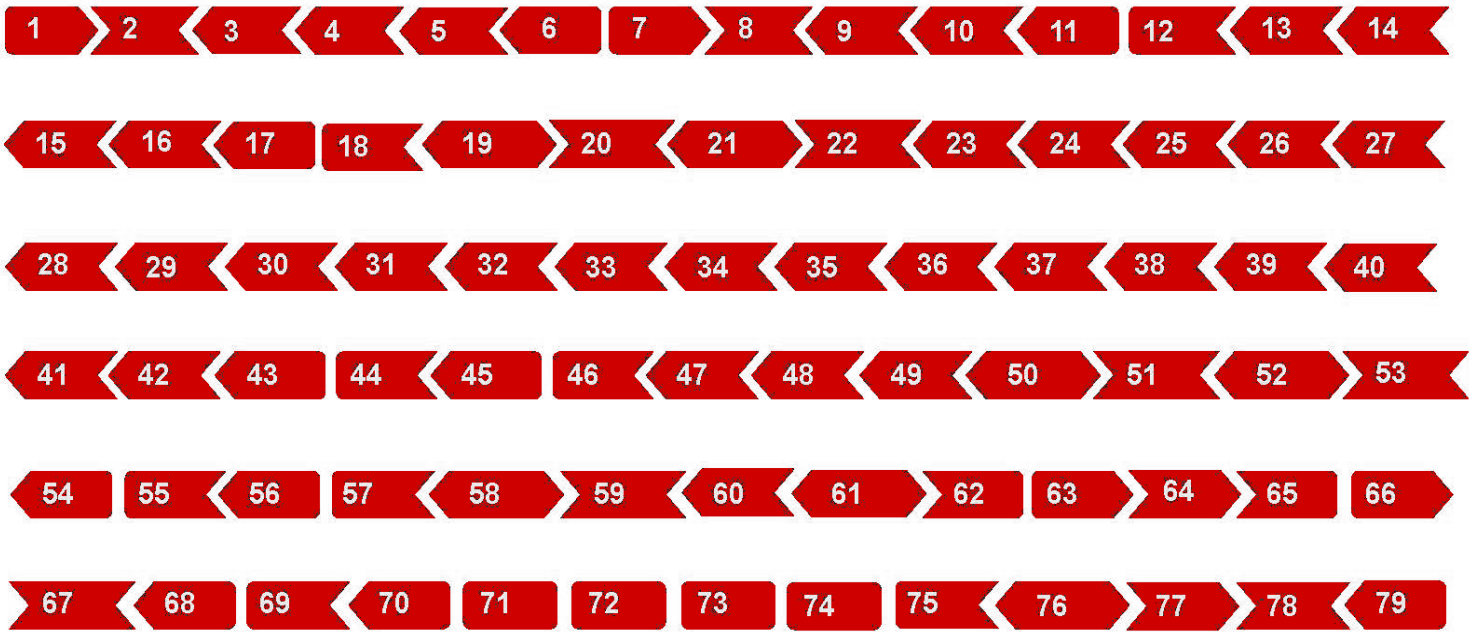


Background: the *DMD* gene

The DMD gene has 79 exons…
but what is an exon?



DMD Gene Exons



Types of Changes in the *DMD* gene

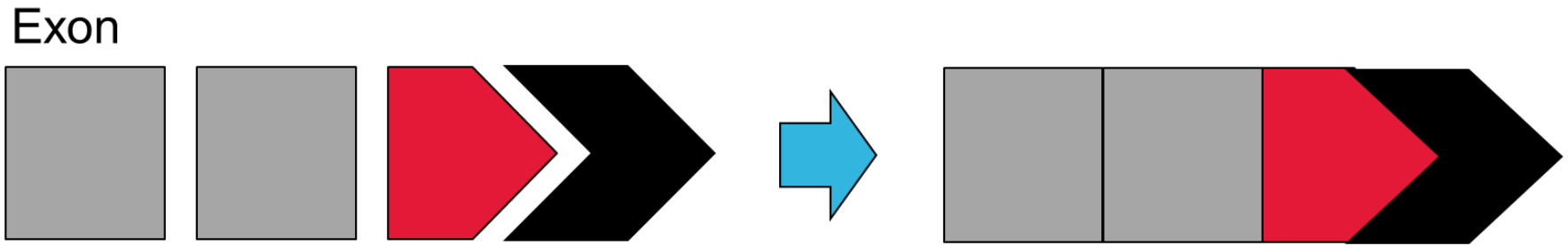
- More than 4000 unique genetic changes (*aka* mutations, variants)
- Fall into categories

Type of Change	% of Duchenne cases	% of Becker cases
Large deletions	60-70%	80-85%
Large duplications	10%	5-10%
Point mutations and other small changes	15-30%	10-15%

Types of Genetic Variants

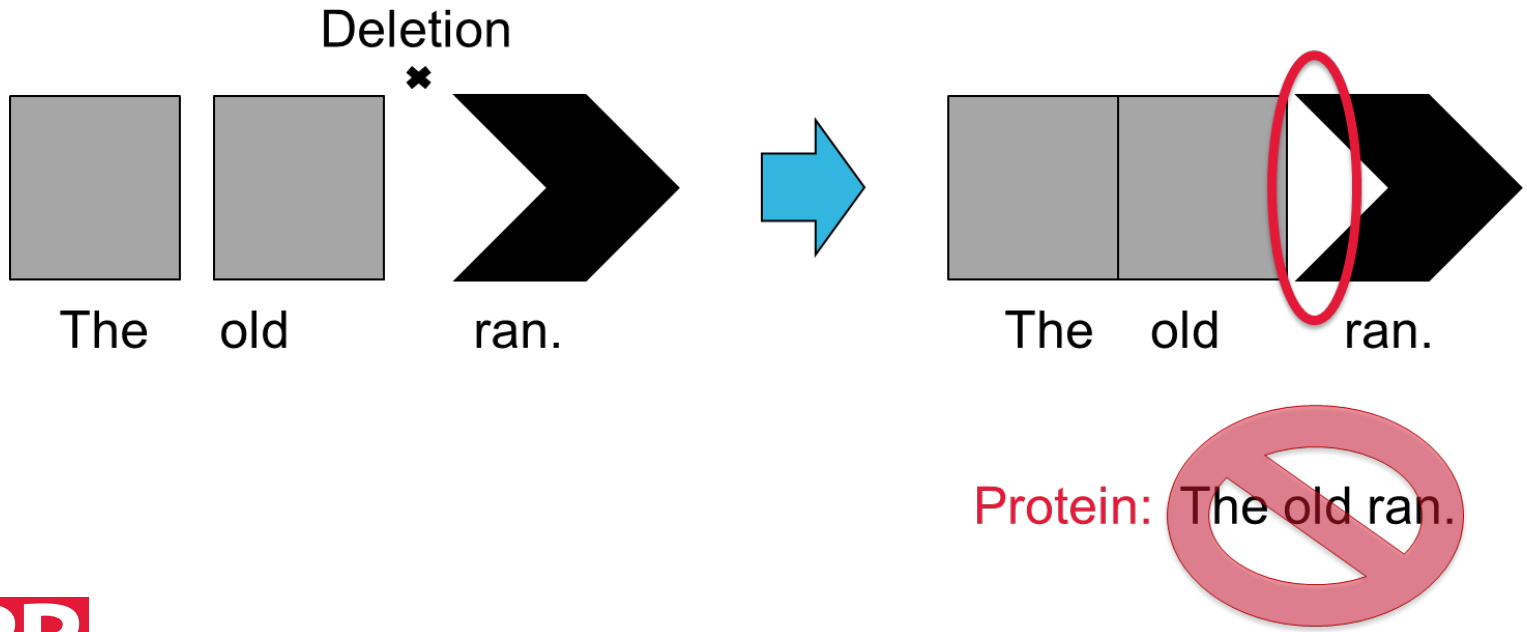
The old dog ran too far.	Original
The old ___ ran too far.	Deletion
The old dog dog ran too far.	Duplication
The old.	Nonsense
The old dog ran too fat.	Missense
The old dog ran too way far.	Insertion

Making Dystrophin: The Reading Frame Rule

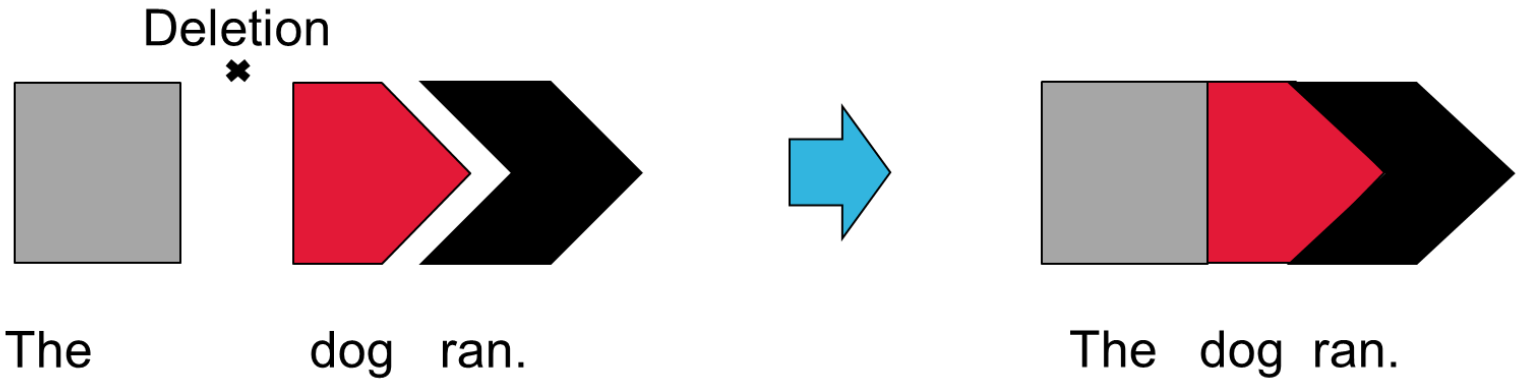


Protein: The old dog ran.

Reading Frame: Out-of-Frame - Duchenne



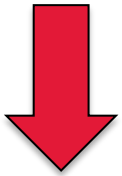
Reading Frame: In-Frame - Becker



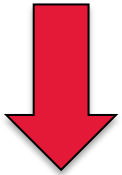
Protein: The dog ran.

Does my variant predict the severity?

Out of frame deletion

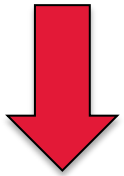


No dystrophin

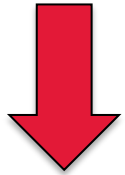


Duchenne

In frame deletion

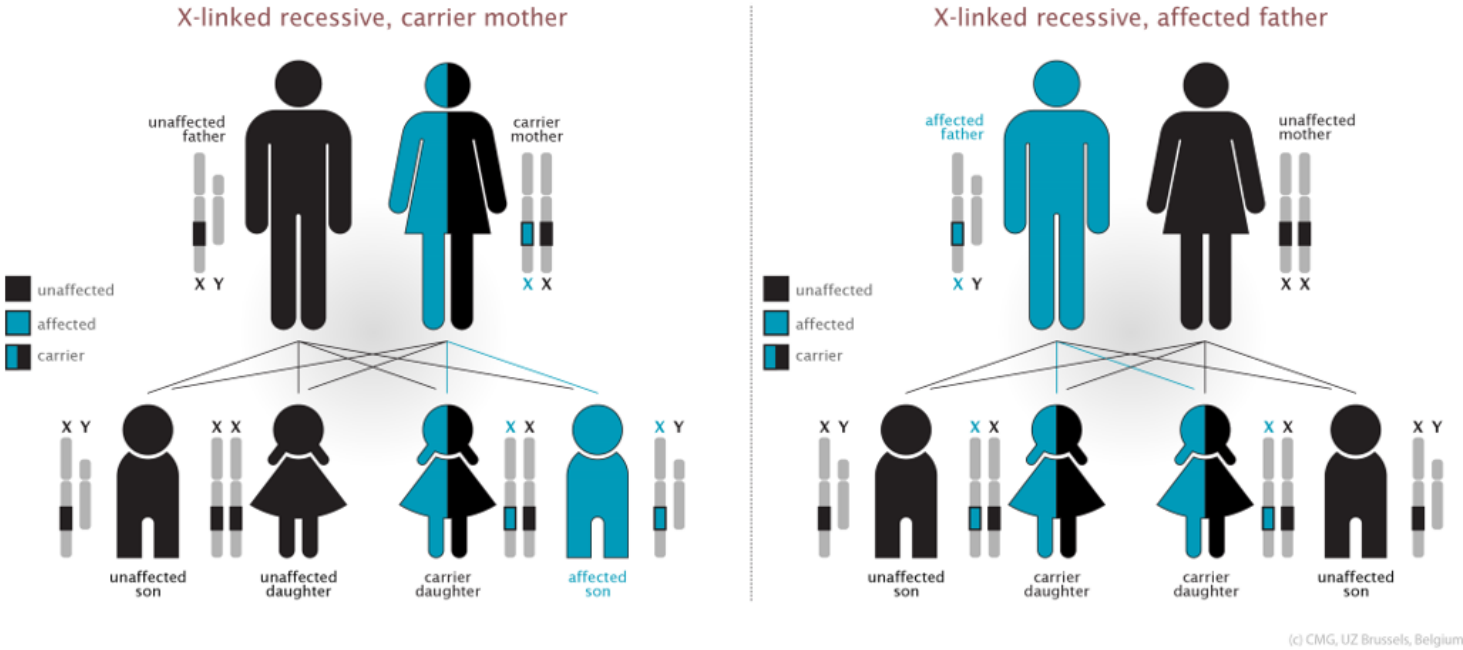


Partially functional dystrophin

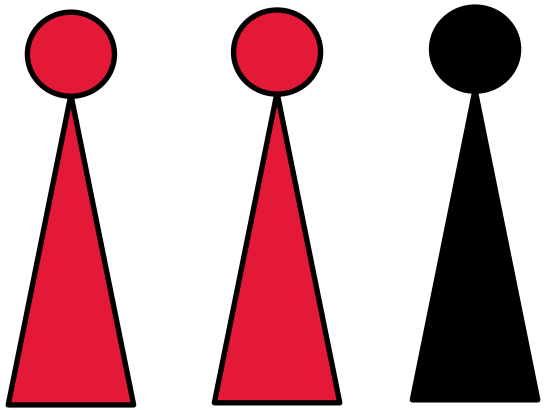


Becker

X-linked Recessive Inheritance



If I don’t have any family history of Duchenne, what are the chances I am a carrier?



About 70% of boys with Duchenne have a mother who carries the mutation. The other 30% of mothers are NOT carriers.

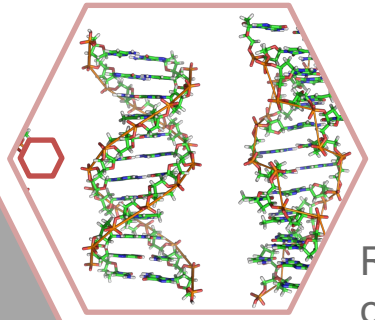
Why is it important to know if I am a carrier?

- Family planning and determining risk for other family members
- Some carriers have symptoms and may need additional support or care
  - Manifesting carrier or female with dystrophinopathy
- Carriers have an increased risk of heart disease and should have screening in early adulthood

How genetics shapes the story…

And 3 reasons why testing is important

Genetic testing is the gold standard for diagnosis



Diagnosis

Results help other family members get testing

Family

Research

Variant-specific therapies are in development

Variant Specific Therapies

- **For Nonsense Variants:**
  -Nonsense read-through
  - PTC Therapeutics (Translarna™)
- **For Deletions**
  -Exon skipping
  - Sarepta Therapeutics (exon 51: Exondys 51™)
  - Sarepta Therapeutics (exon 53: Vyondys 53™)
  - NS Pharma (exon 53: Viltepso™)
  - Sarepta Therapeutics (exon 45: Amondys 45™)
- **Gene Therapy**

Roles of PPMD Genetic Counselors

THE DUCHENNE REGISTRY

DECODE DUCHENNE

Free genetic testing and counseling for Duchenne and Becker muscular dystrophy

Parent Project Muscular Dystrophy

???

PPMD

DECODE DUCHENNE

Free genetic testing and counseling for Duchenne and Becker muscular dystrophy

Parent Project Muscular Dystrophy
JOIN THE FIGHT. END DUCHENNE.

SAREPTA THERAPEUTICS

PTC THERAPEUTICS

VERTEX
THE SCIENCE of POSSIBILITY

NS Pharma

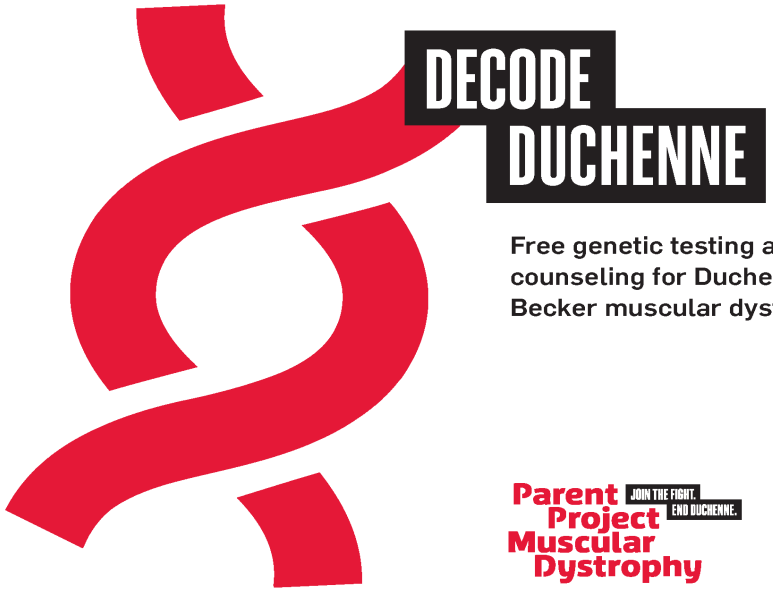
DECODE DUCHENNE

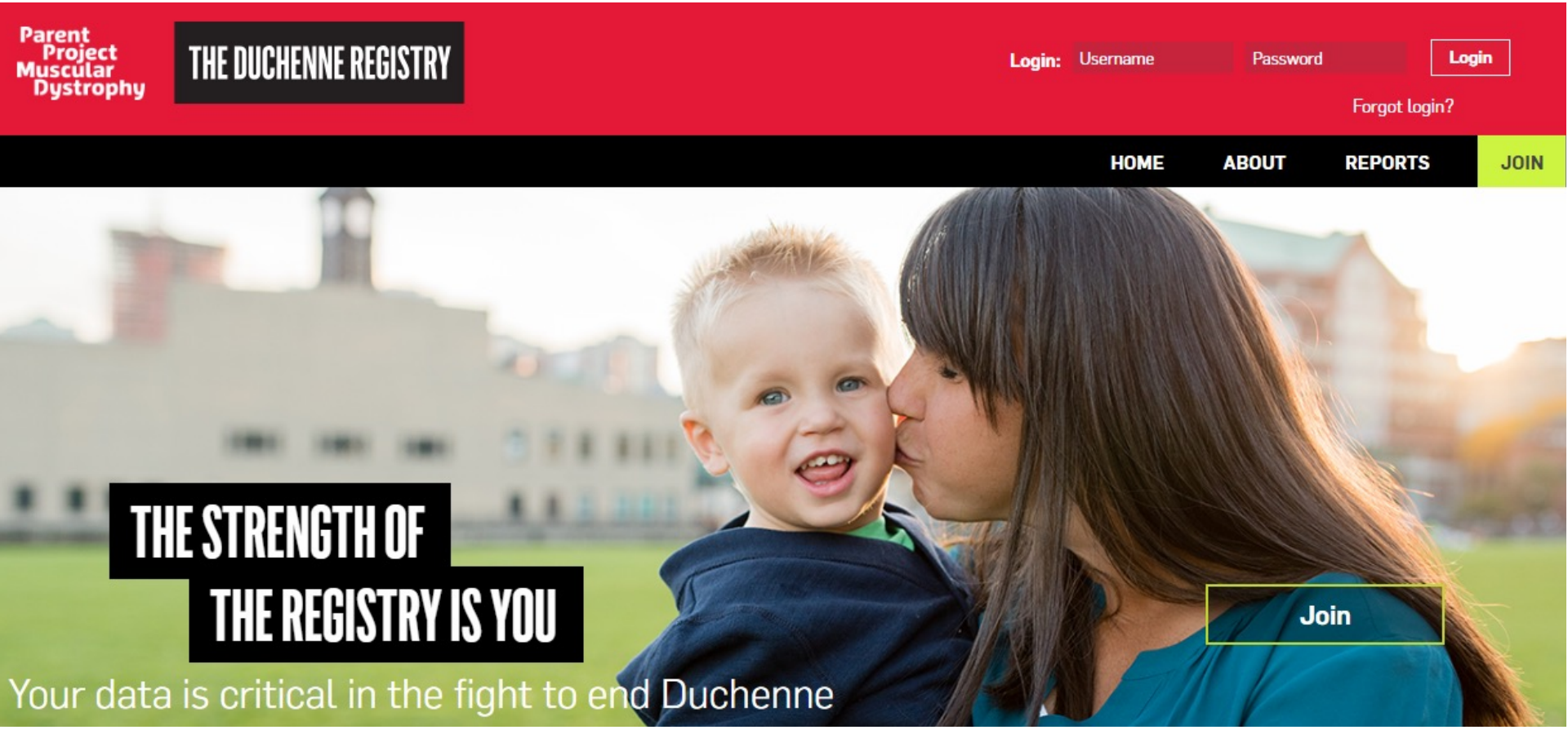
Criteria for Free Testing:

- ☑ Male with a confirmed or suspected diagnosis of Duchenne or Becker,
  OR
  Female with a relative with Duchenne or Becker
- ☑ Never had genetic testing OR previous genetic testing has not confirmed a variant OR past testing could not determine border of deletion/duplication
- ☑ Legal resident of US or Canada

All testing performed at: revvity

Over 2,500 patients tested through the Decode Duchenne program!

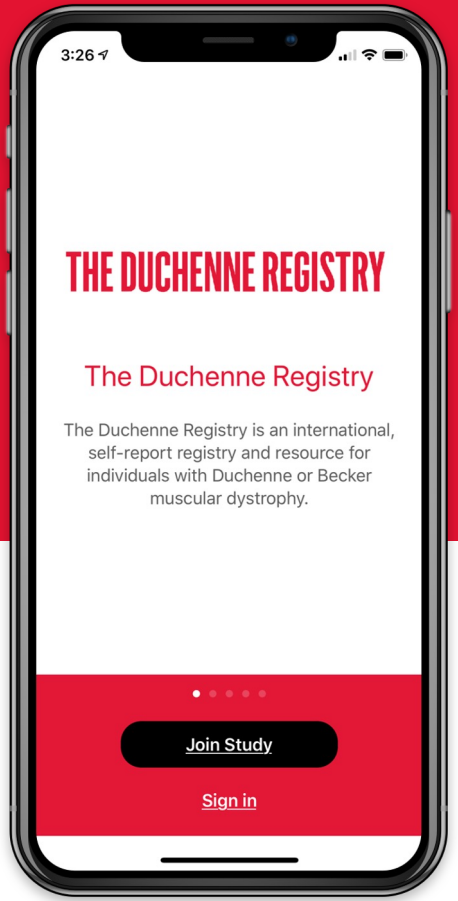



Parent Project Muscular Dystrophy
THE DUCHENNE REGISTRY
Login:
Username
Password
Login
Forgot login?
HOME
ABOUT
REPORTS
JOIN
THE STRENGTH OF
THE REGISTRY IS YOU
Your data is critical in the fight to end Duchenne
Join

Our Impact


5500+
Registrations since launch
115+
Countries Represented
15YRS
of Longitudinal Data
100+
Trials & Studies Recruited

The Duchenne Registry App



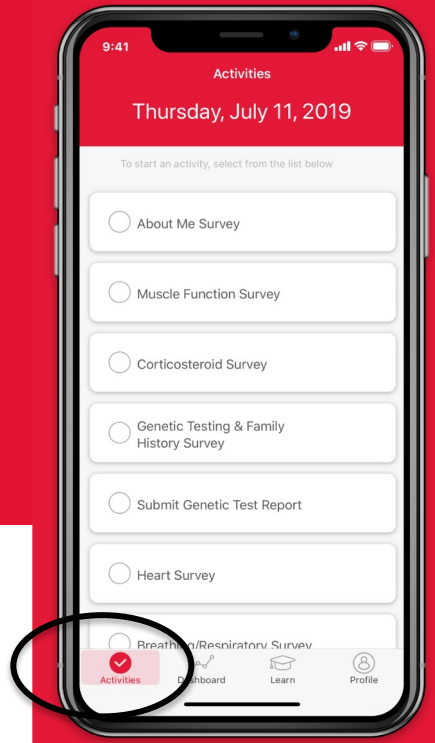
Convenient App Platform

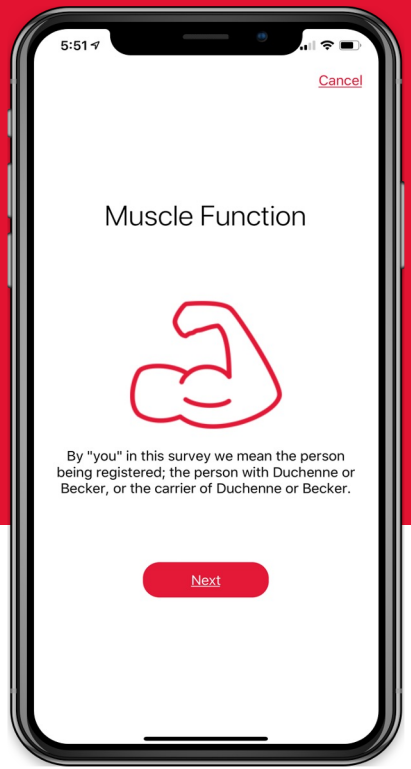
PPMD

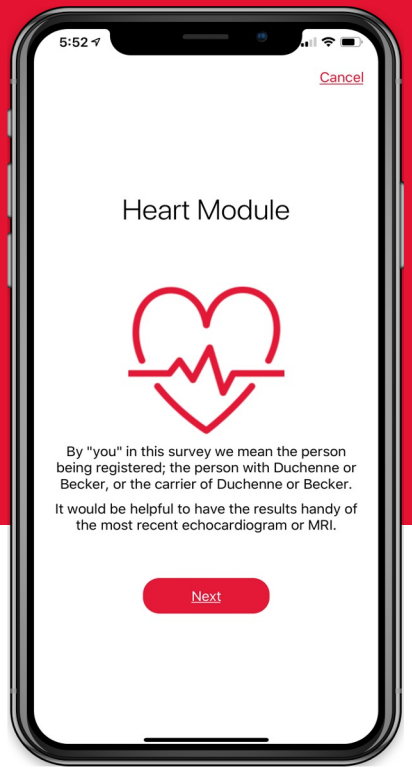
The Duchenne Registry App

E-Signature Consent Form

The Duchenne Registry App







Why YOU should join the Registry

1. Be a citizen scientist
2. Get specific information on clinical trials and drug approvals
3. Better understanding of EVERYONE with Duchenne/Becker/Carriers

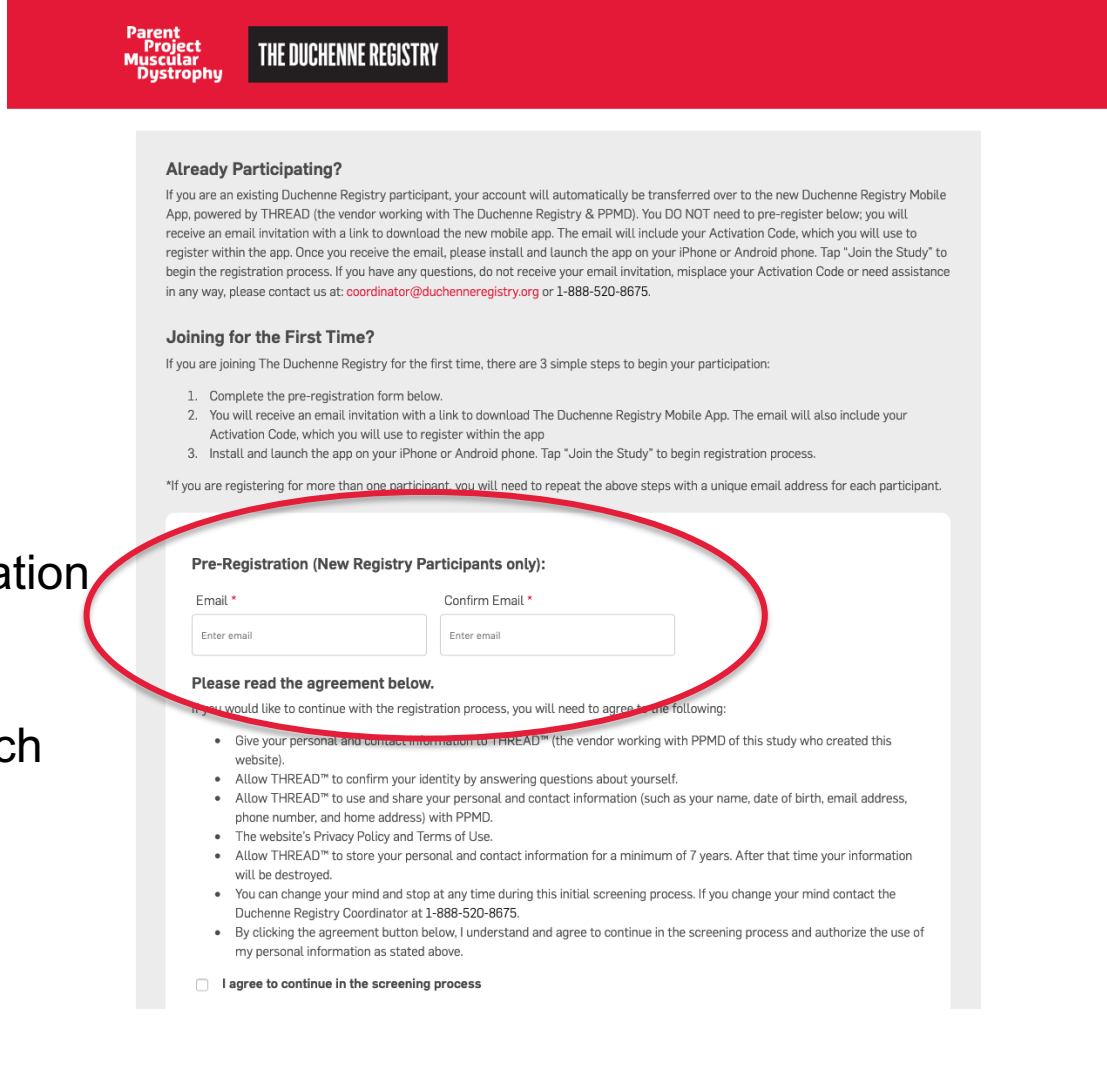
ALL New Registrants:

Go to www.DuchenneRegistry.org

Click “**JOIN**”

Enter your email under Pre-Registration

Invitation email will come from no-reply@threadresearch.com, which will contain link & activation code.



Thank you!

coordinator@parentprojectmd.org

888-520-8675