

Genetics, The Duchenne Registry And Your Family

Parent JOIN THE FIGHT.
END DUCHENNE.
**Project
Muscular
Dystrophy**

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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!



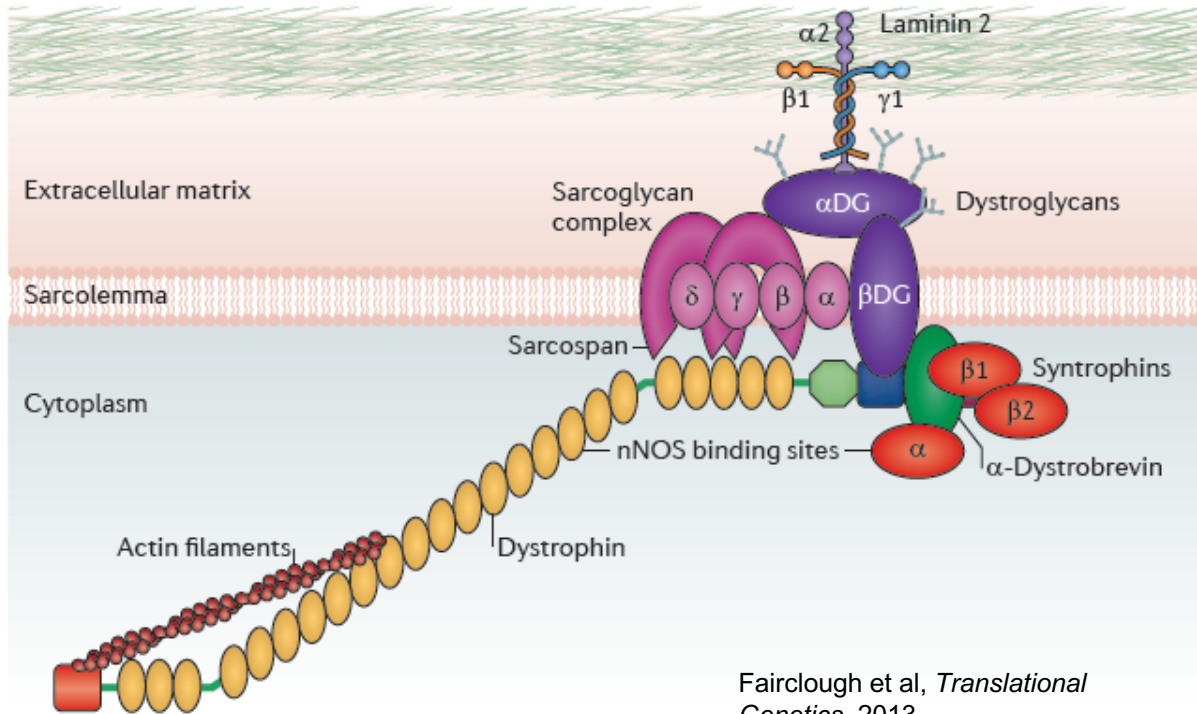
What is Duchenne?

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.

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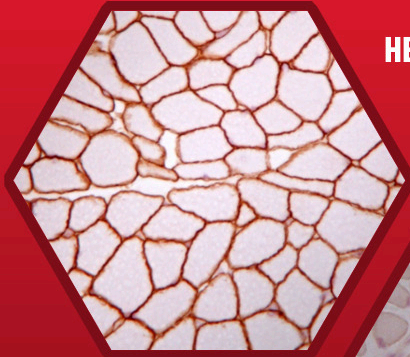
Duchenne and Becker are dystrophinopathies



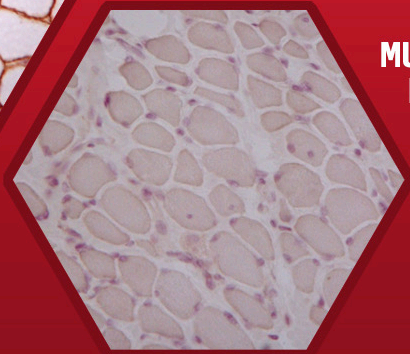
Fairclough et al, *Translational Genetics*, 2013

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.

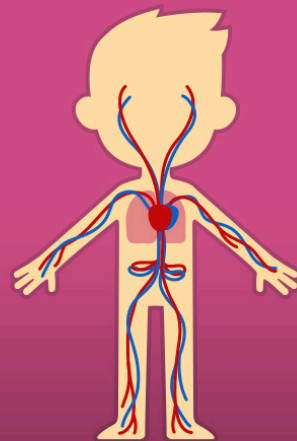
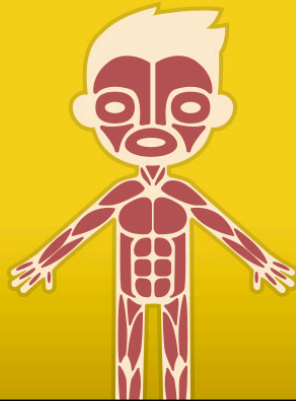
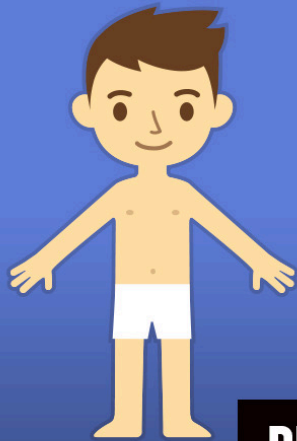


HEALTHY MUSCLE TISSUE

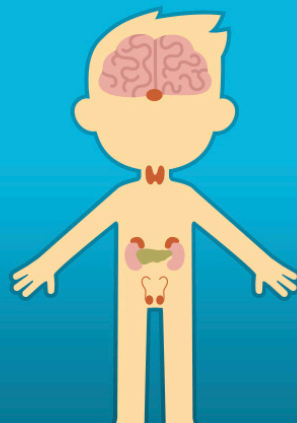
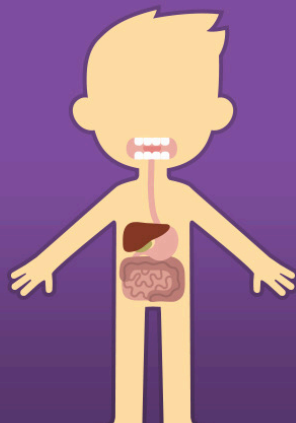
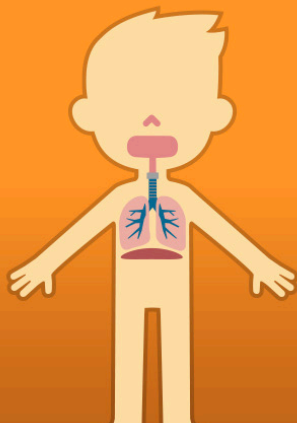


**MUSCLE TISSUE WITH
DUCHENNE MUSCULAR DYSTROPHY**

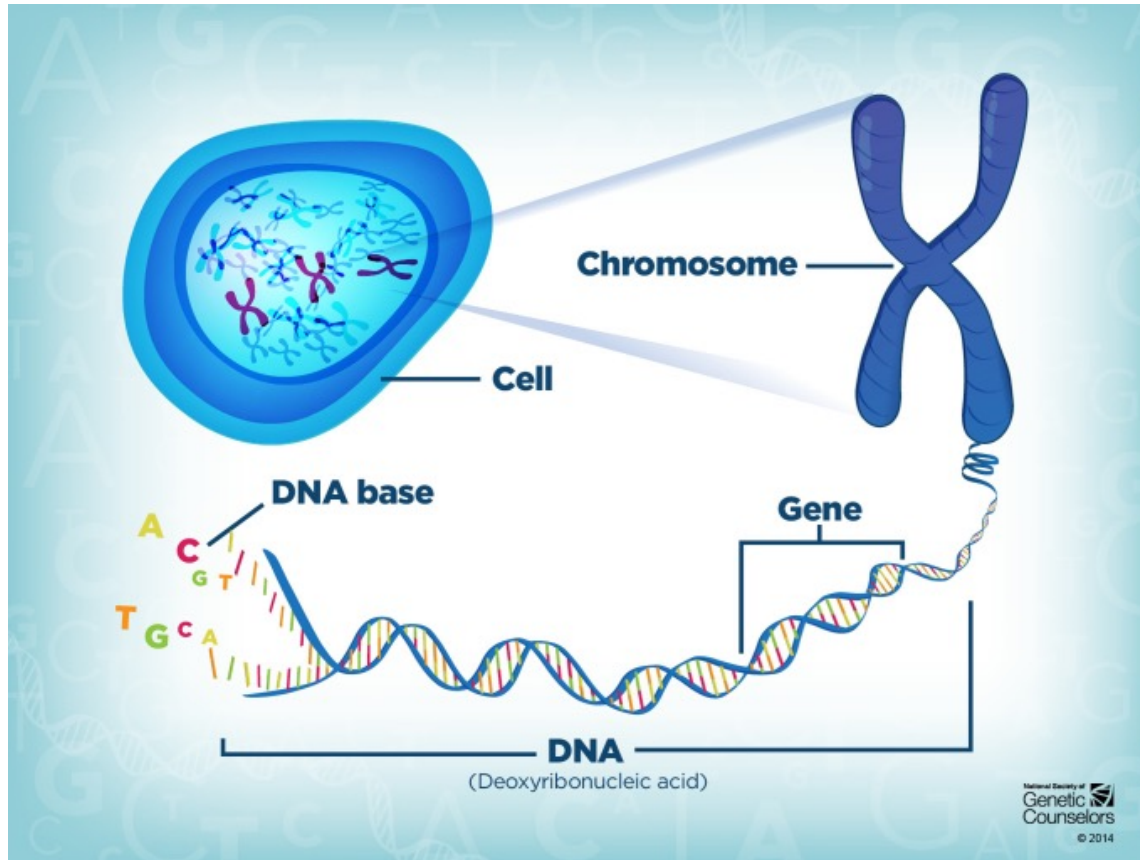




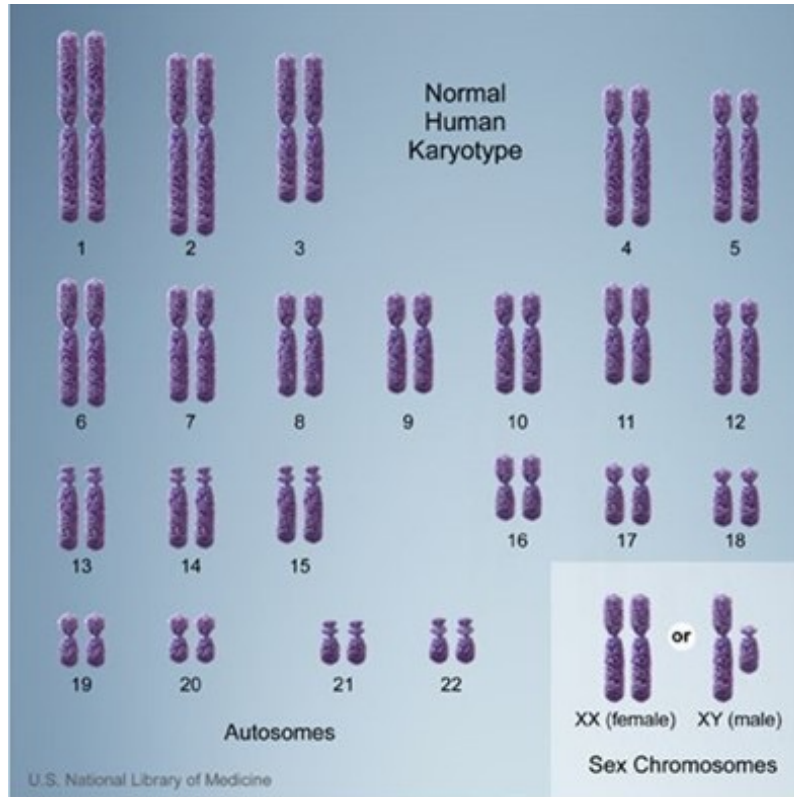
**DUCHENNE IS NOT JUST A DISEASE OF THE MUSCLES.
IT AFFECTS EVERY SYSTEM IN THE HUMAN BODY.**



Genetics Review

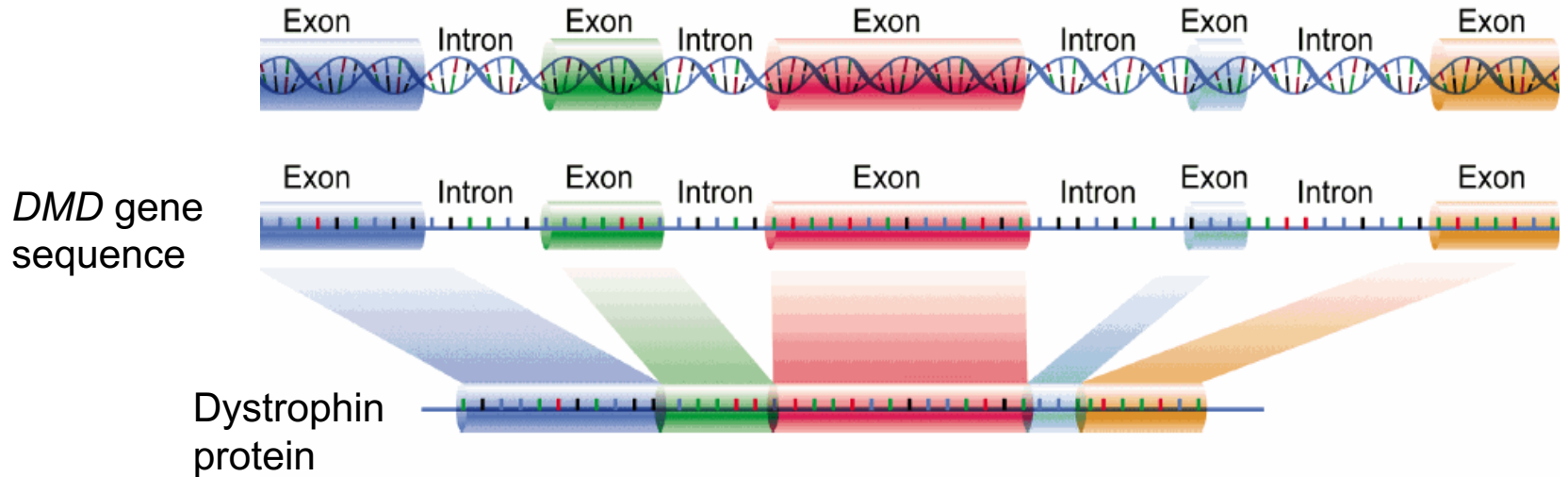


Typical Human Karyotype

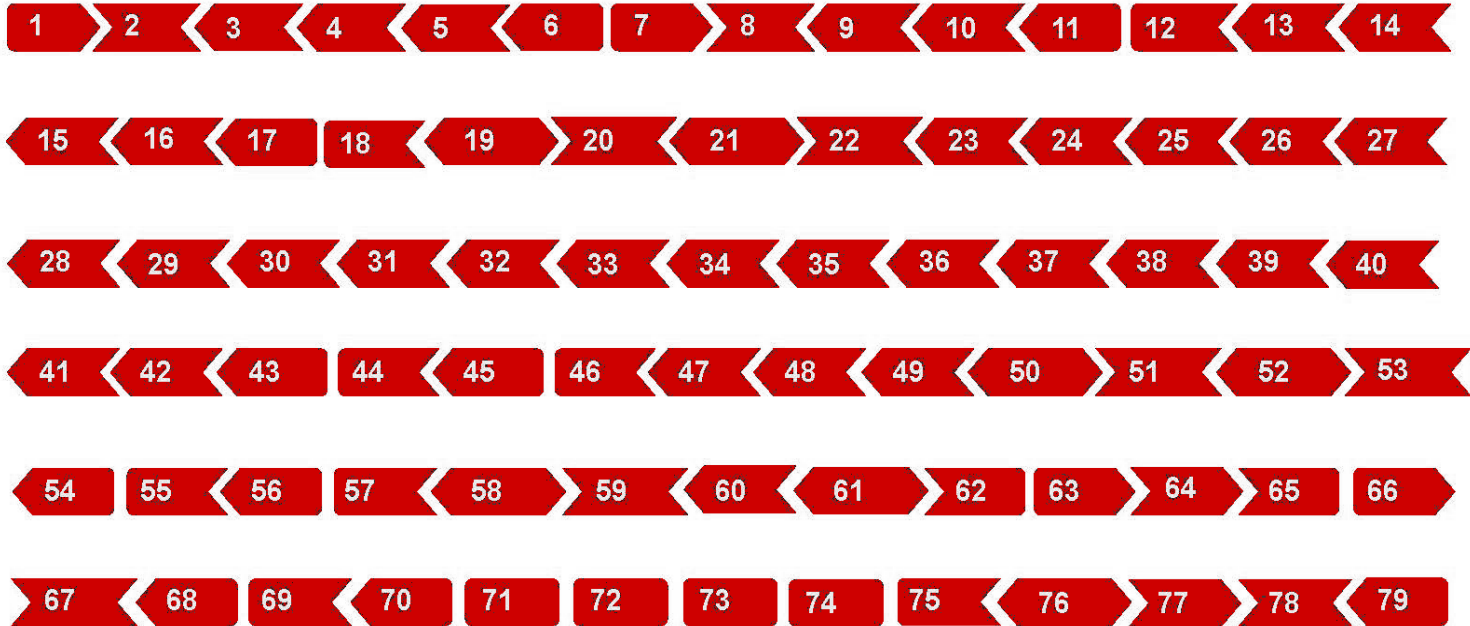


Background: the *DMD* gene

*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



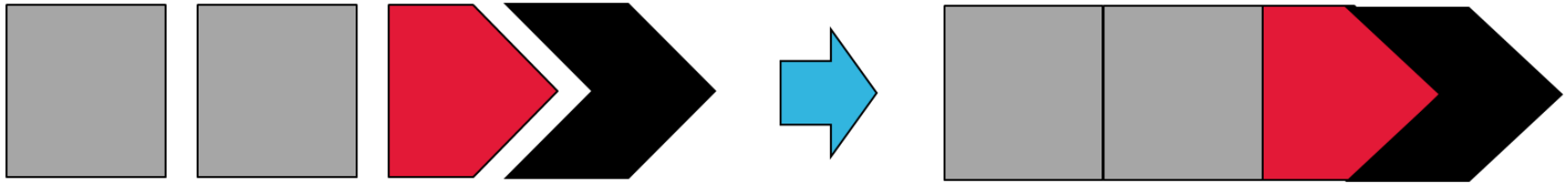
Type of Change	% of Duchenne cases	% of Becker cases
Large deletions	60-70%	80-85%
Large duplications	10%	5-10%
Point mutations and other small changes	15-30%	10-15%

Types of Genetic Variants

The old dog ran too far.	Original
The old <u> </u> 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

Exon

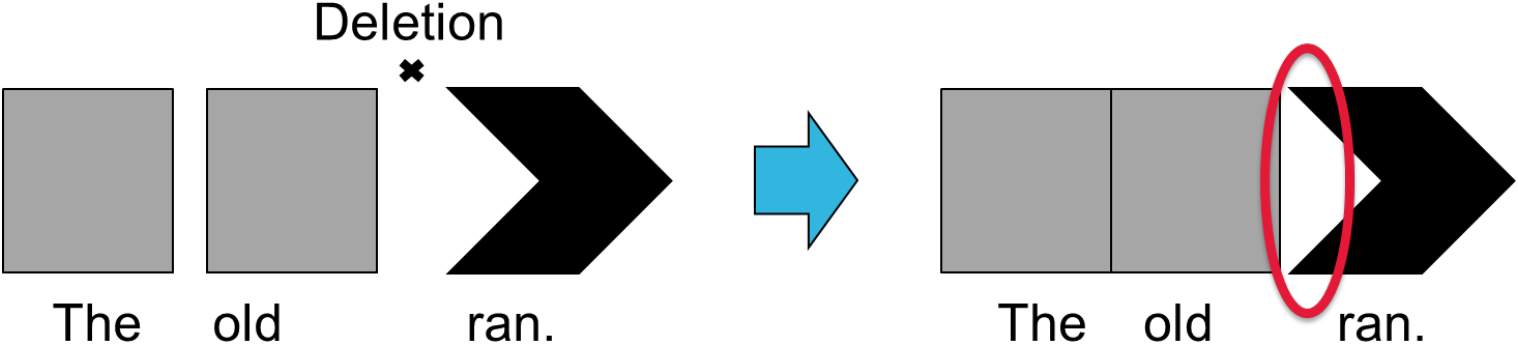


The old dog ran.

The old dog ran.

Protein: The old dog ran.

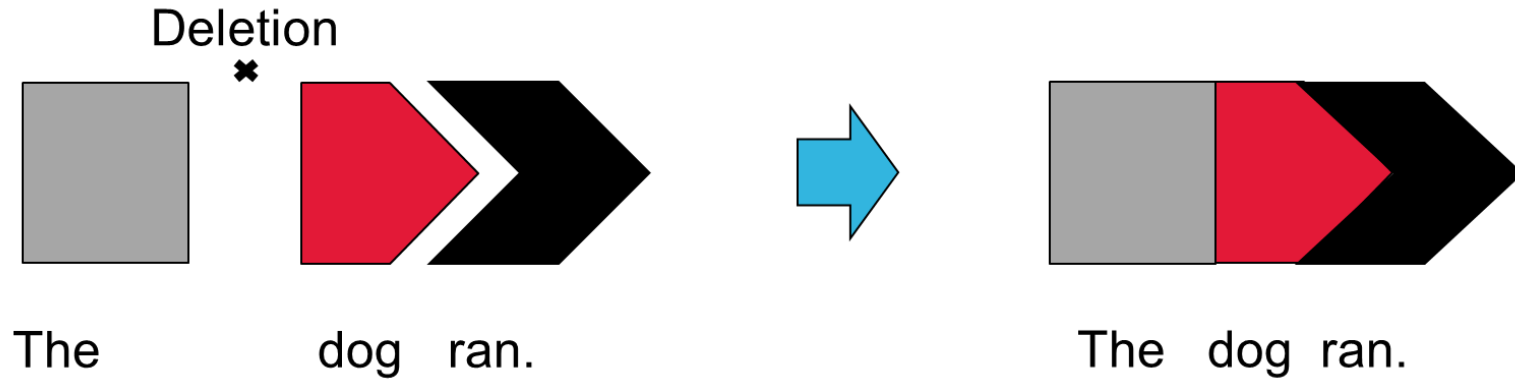
Reading Frame: Out-of-Frame - Duchenne



Protein: ~~The old ran.~~



Reading Frame: In-Frame - Becker



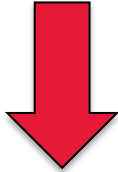
Protein: The dog ran.

Does my variant predict the severity?

Out of frame deletion



No dystrophin



Duchenne

In frame deletion

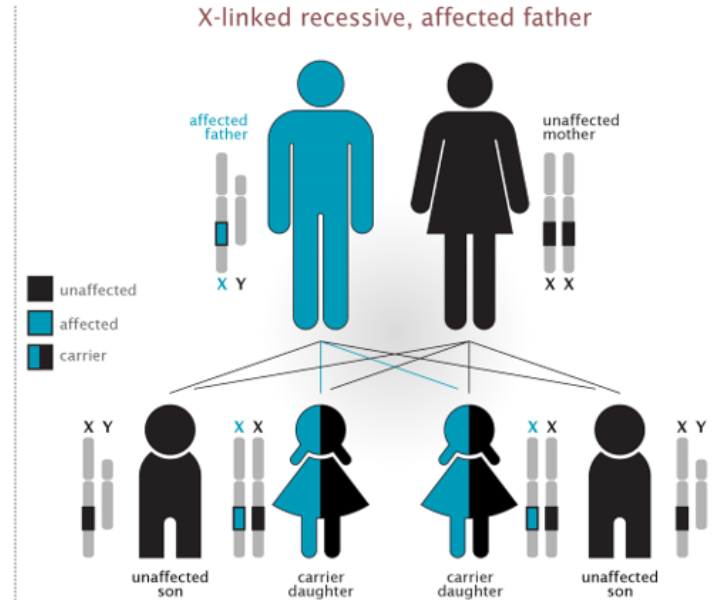
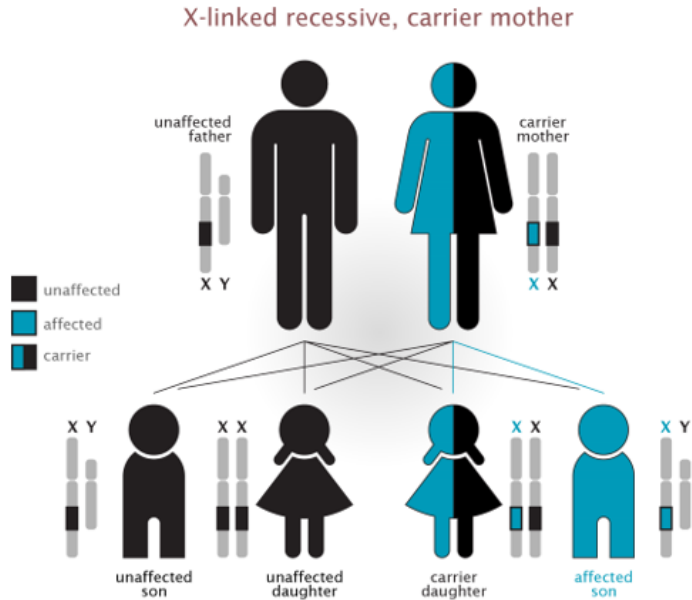


Partially functional dystrophin

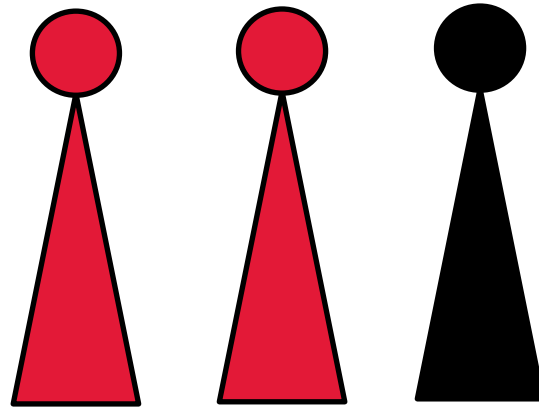


Becker

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?

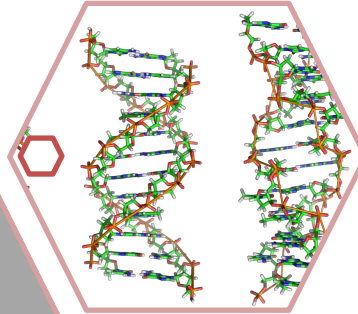
- Family planning and determining risk for other family members
- Some carriers have symptoms and may need additional support or care
 - Manifesting carrier or female with dystrophinopathy
- Carriers have an increased risk of heart disease and should have screening in early adulthood

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



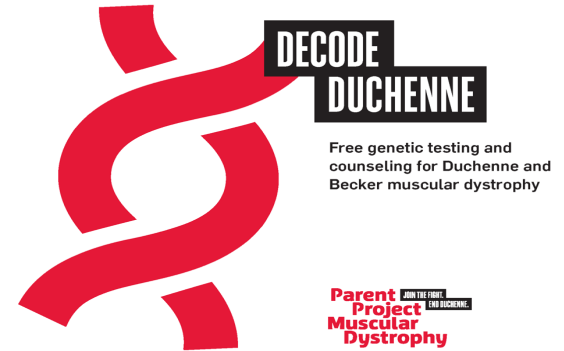
Research

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





DECODE DUCHENNE

Free genetic testing and
counseling for Duchenne and
Becker muscular dystrophy

**Parent Project
Muscular
Dystrophy** JOIN THE FIGHT.
END DUCHENNE.



DECODE DUCHENNE

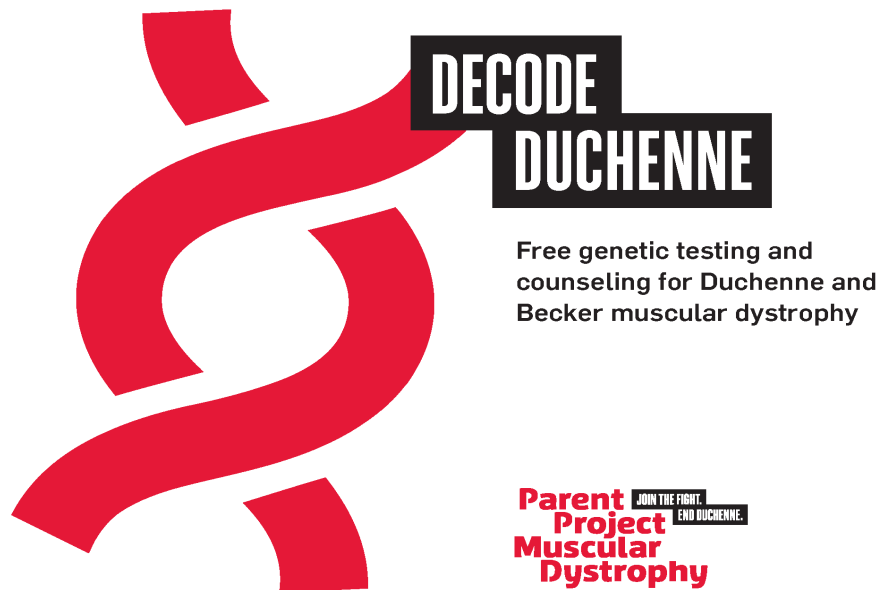
Criteria for Free Testing:

- ☑ 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:



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



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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**



The Duchenne Registry App

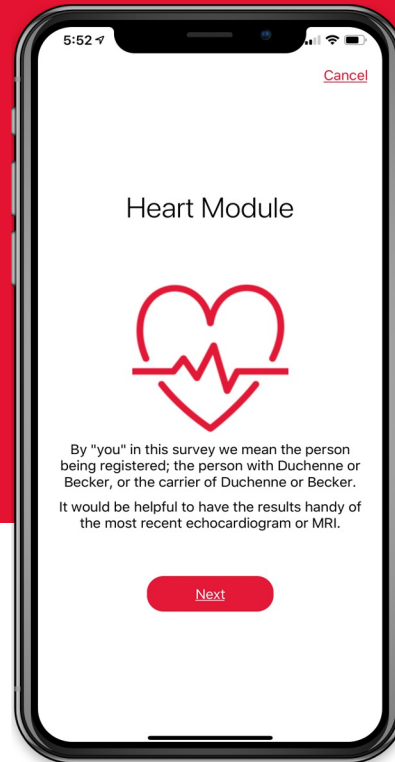
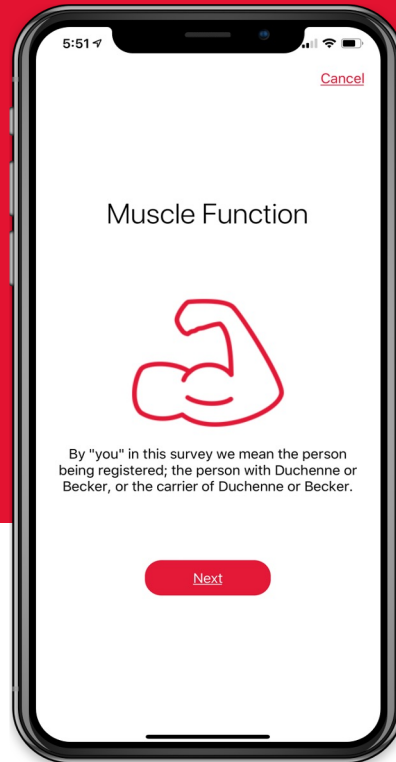
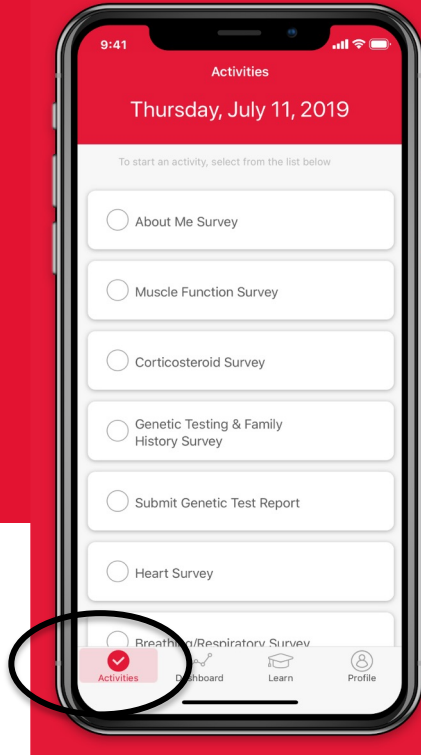
The image displays two sequential screens of the Duchenne Registry App's e-signature consent form. The left screen, titled 'Consent', shows the introductory text and input fields for 'First Name' and 'Last Name'. The right screen, also titled 'Consent', shows the 'Signature' section with a handwritten signature and a 'Clear' button.

Screen 1 (Left): The screen is titled 'Consent' with a back arrow on the left and a 'Cancel' button on the right. The text reads: "By providing your name and signature, you confirm that you read the information contained herein and that you wish to take part in this research study." Below the text are two input fields labeled 'First Name' and 'Last Name'. At the bottom, there is a 'Next' button.

Screen 2 (Right): The screen is also titled 'Consent' with a back arrow on the left and a 'Cancel' button on the right. The text reads: "Signature" followed by "By providing your name and signature, you confirm that you read the information contained herein and that you wish to take part in this research study." Below this is the instruction: "Please sign using your finger on the line below." A handwritten signature is visible on a horizontal line. Below the signature is a 'Clear' button. At the bottom, there is a 'Done' button.

**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.

Already Participating?

If you are an existing Duchenne Registry participant, your account will automatically be transferred over to the new Duchenne Registry Mobile App, powered by THREAD (the vendor working with The Duchenne Registry & PPMMD). You DO NOT need to pre-register below; you will receive an email invitation with a link to download the new mobile app. The email will include your Activation Code, which you will use to register within the app. Once you receive the email, please install and launch the app on your iPhone or Android phone. Tap "Join the Study" to begin the registration process. If you have any questions, do not receive your email invitation, misplace your Activation Code or need assistance in any way, please contact us at: coordinator@duchenneregistry.org or 1-888-520-8675.

Joining for the First Time?

If you are joining The Duchenne Registry for the first time, there are 3 simple steps to begin your participation:

1. Complete the pre-registration form below.
2. You will receive an email invitation with a link to download The Duchenne Registry Mobile App. The email will also include your Activation Code, which you will use to register within the app
3. Install and launch the app on your iPhone or Android phone. Tap "Join the Study" to begin registration process.

*If you are registering for more than one participant, you will need to repeat the above steps with a unique email address for each participant.

Pre-Registration (New Registry Participants only):

Email *

Enter email

Confirm Email *

Enter email

Please read the agreement below.

If you would like to continue with the registration process, you will need to agree to the following:

- Give your personal and contact information to THREAD™ (the vendor working with PPMMD of this study who created this website).
- Allow THREAD™ to confirm your identity by answering questions about yourself.
- Allow THREAD™ to use and share your personal and contact information (such as your name, date of birth, email address, phone number, and home address) with PPMMD.
- The website's Privacy Policy and Terms of Use.
- Allow THREAD™ to store your personal and contact information for a minimum of 7 years. After that time your information will be destroyed.
- You can change your mind and stop at any time during this initial screening process. If you change your mind contact the Duchenne Registry Coordinator at 1-888-520-8675.
- By clicking the agreement button below, I understand and agree to continue in the screening process and authorize the use of my personal information as stated above.

I agree to continue in the screening process

Thank you!

coordinator@parentprojectmd.org

888-520-8675