Genetics, The Duchenne Registry And Your Family

Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

Kevin Counterman

November 17, 2018

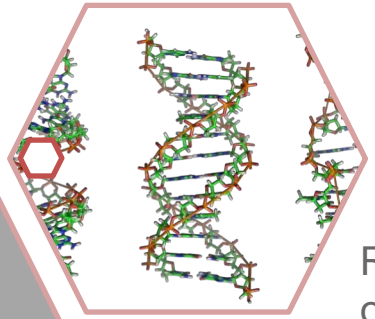
Topics for Today:

1. Importance of genetics in Duchenne and Becker
2. Free genetic testing through Decode Duchenne
3. Connecting to research through The Duchenne Registry
4. Answer your questions!

How genetics shapes the story…

And 3 reasons why testing is important

Genetic testing is the gold standard for diagnosis



Diagnosis

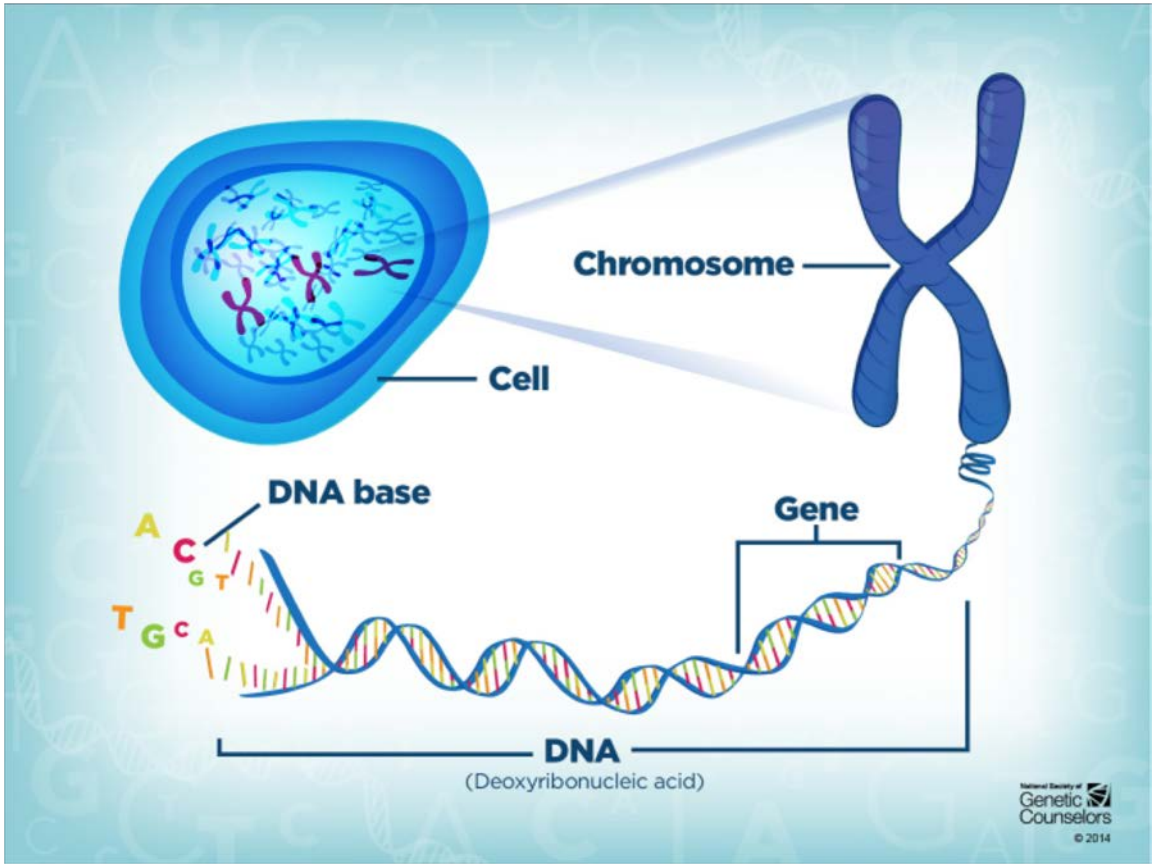
Results help other family members get testing

Family

Research

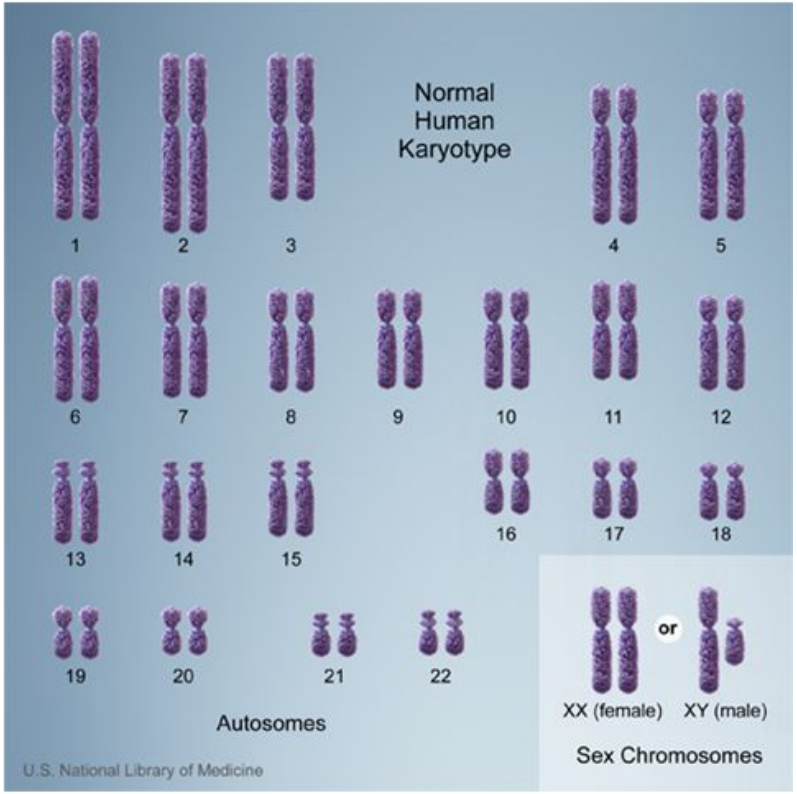
Mutation-specific therapies are in development

Genetics Review

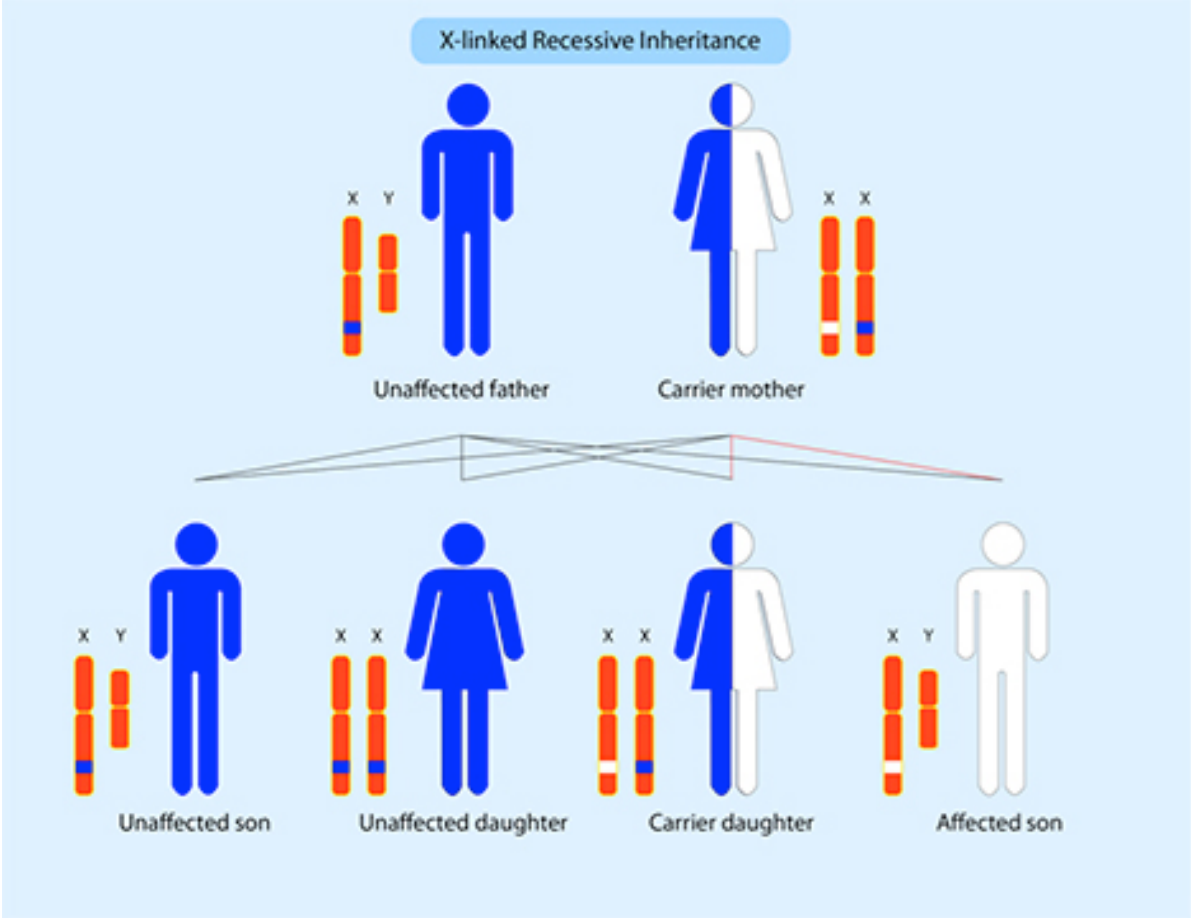


Normal Human Karyotype

- The chromosomes in a human karyotype are arranged in **homologous pairs.**
- The first **22** pairs of chromosomes are called **autosomes.**
- The **23rd** pair of chromosomes are known as the **sex chromosomes**.



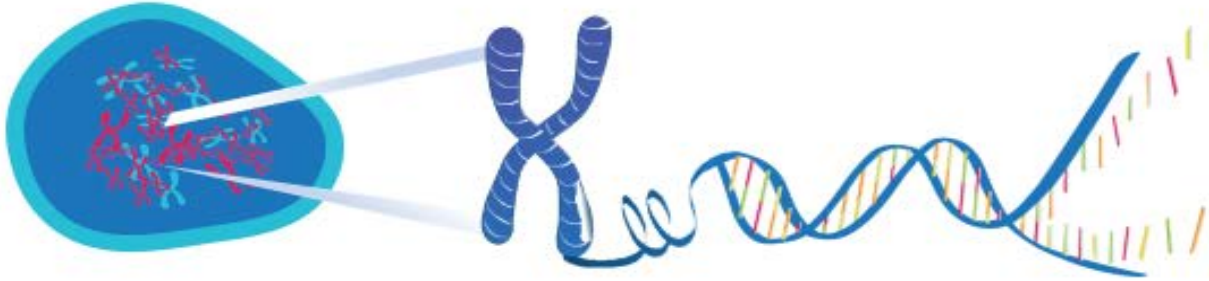
X-linked Recessive Inheritance



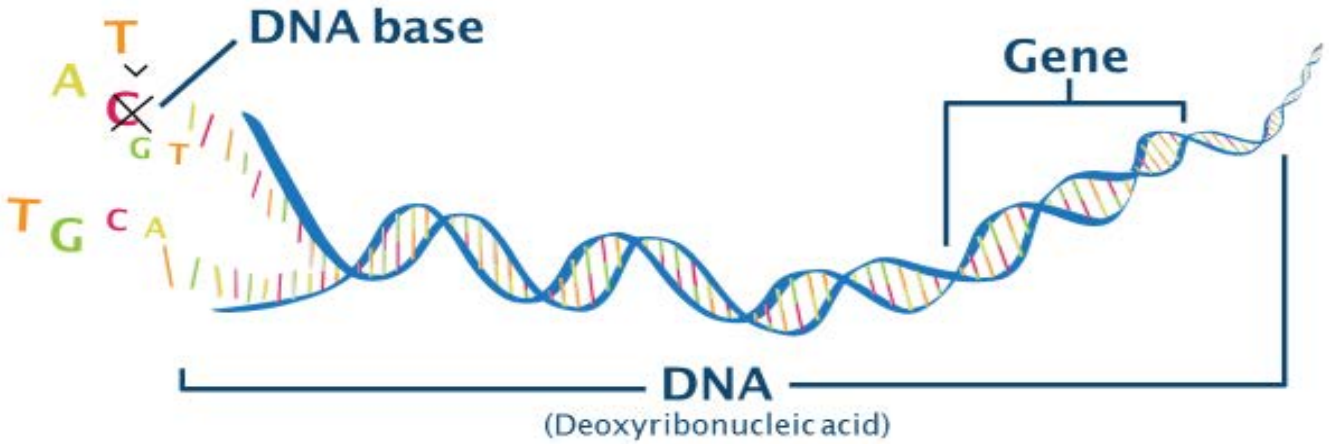
BOOK - GENOME

CHAPTERS - CHROMOSOMES

SENTENCE - GENE



National Society of Genetic Counselors
©2014



The gray cat ran down the hall.

The gray cat ran down the ball.

Changes in DNA might change the way a gene works.

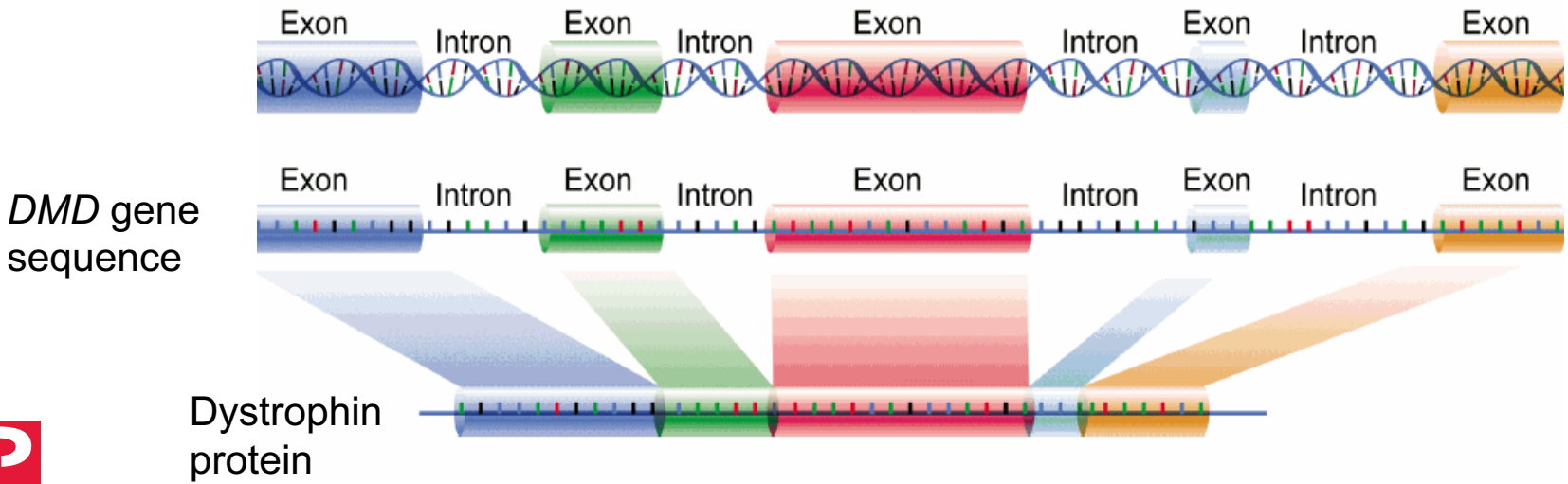
National Society of Genetic Counselors
©2014

Types of Genetic Mutations

The gray cat ran down the hall.	**Original**
The gray cat ran down the ball.	**Missense**
The gray green cat ran down the hall.	**Insertion**
The gray ___ ran down the hall.	**Deletion**
The gray cat cat ran down the hall.	**Duplication**
The gray.	**Nonsense**

Background: the *DMD* gene

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



Types of Changes in the *DMD* gene

- More than 4000 unique genetic changes
- 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%

Out-of-frame vs. In-frame

- Letters in the DNA sequence must stay in groups of three:

AAC ATG CGG TAC

- Example sentence: THE OLD DOG RAN TOO FAR

Out-of-frame deletion:

THE OLD DOG RAN TOO FAR

THL DDO GRA NTO OFA R

Duchenne

In-frame deletion:

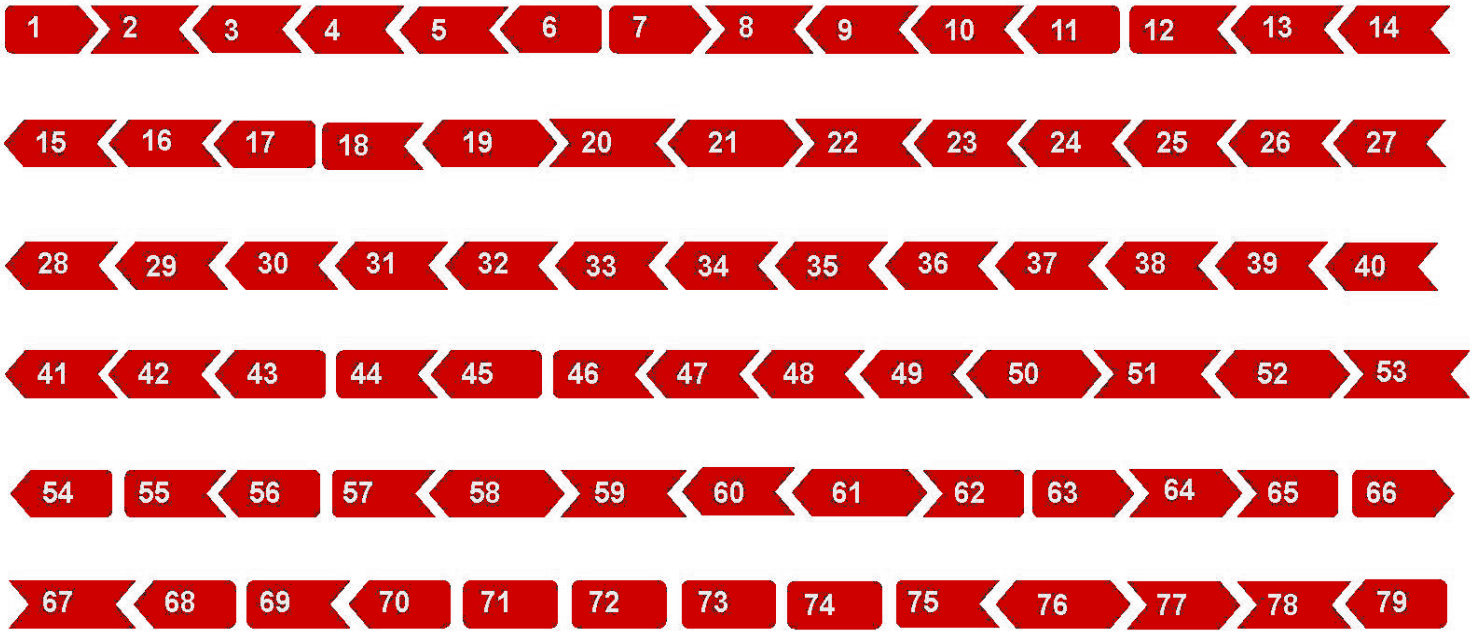
THE OLD DOG RAN TOO FAR

THE OLD RAN TOO FAR

Becker

Large deletions and duplications

- One or more exons are missing or repeated



Why is the type of genetic variant so important?

1. Helps to confirm the **diagnosis**
2. Essential for coordinating testing of **family** members
3. Critical for mutation-specific **research and approved therapies**…new strategies target the specific DNA variant

Mutation-Specific Therapies

- **For Nonsense Mutations:**
  - Nonsense mutation read-through
    - PTC Therapeutics (Translarna®)
- **For Deletions**
  - Exon skipping
    - Sarepta Therapeutics (exon 51: Exondys 51®; exon 45: SRP-4045; exon 53: SRP-4053)
    - NS Pharma (exon 53: NS-065/NCNP-01)
    - Wave Life Sciences (exon 51: WVE-210201)

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

DECODE DUCHENNE

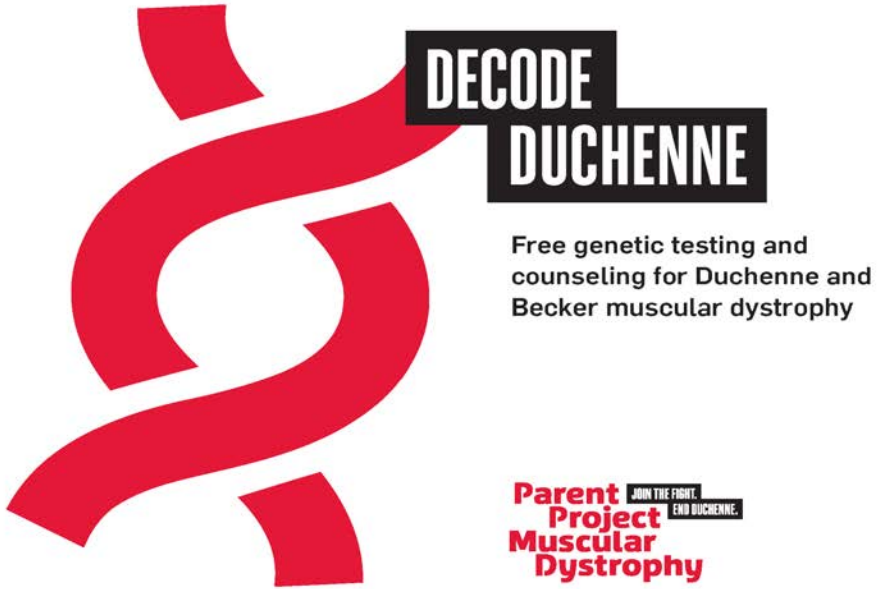
Criteria for Free Testing:

- ☑ Male with a confirmed or suspected diagnosis of Duchenne or Becker,
  OR
  Female with a relative with Duchenne or Becker with a known mutation
- ☑ Never had genetic testing OR previous genetic testing has not confirmed a mutation
- ☑ Any financial barrier
- ☑ Legal resident of US or Canada

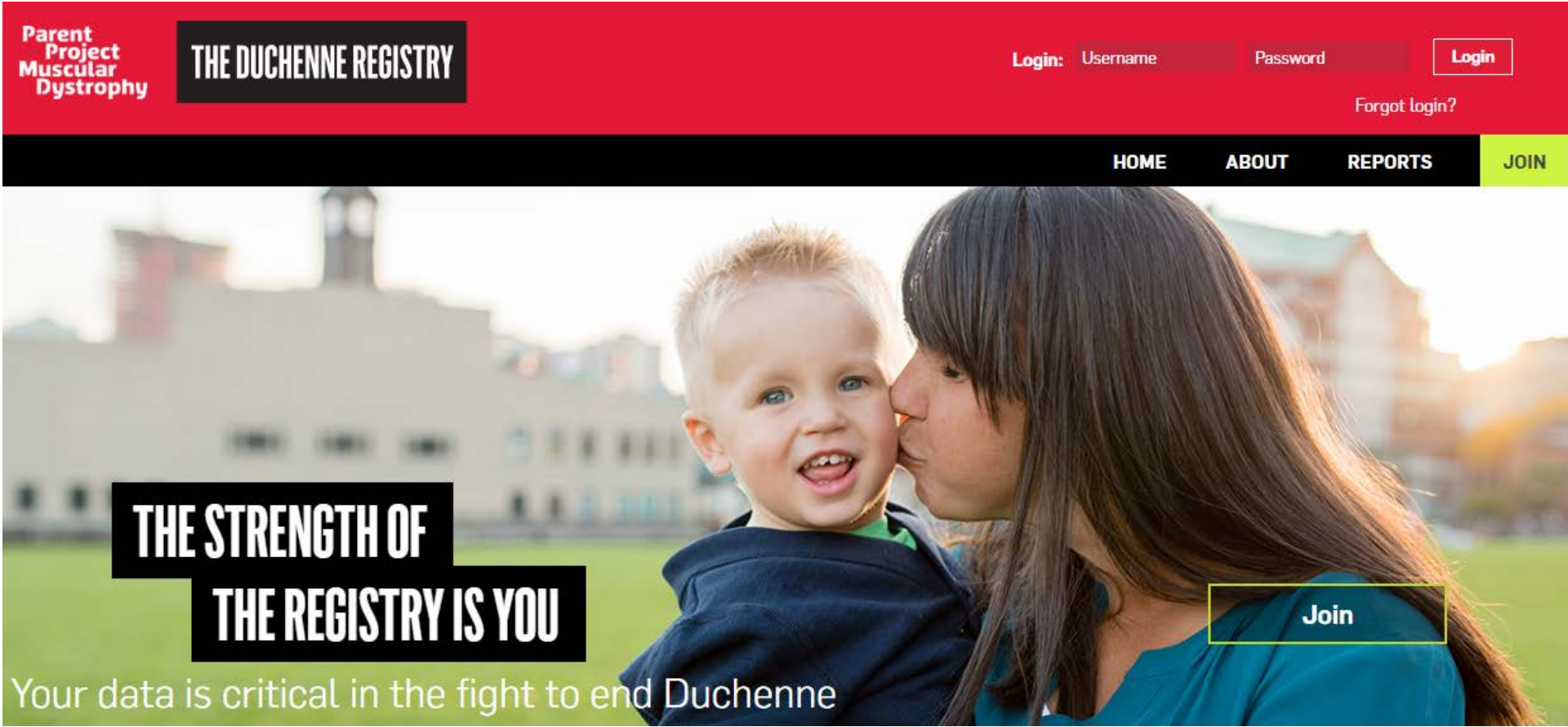
All testing performed at:

PerkinElmer For the Better | PerkinElmer Genetics

Over 1,000 participants to date in the Decode Duchenne program!



New Registry Name and Website!



OUR IMPACT

4336
Total Registrants
113
Countries Represented
60
Trials Recruited
17
Industry Partners
Join

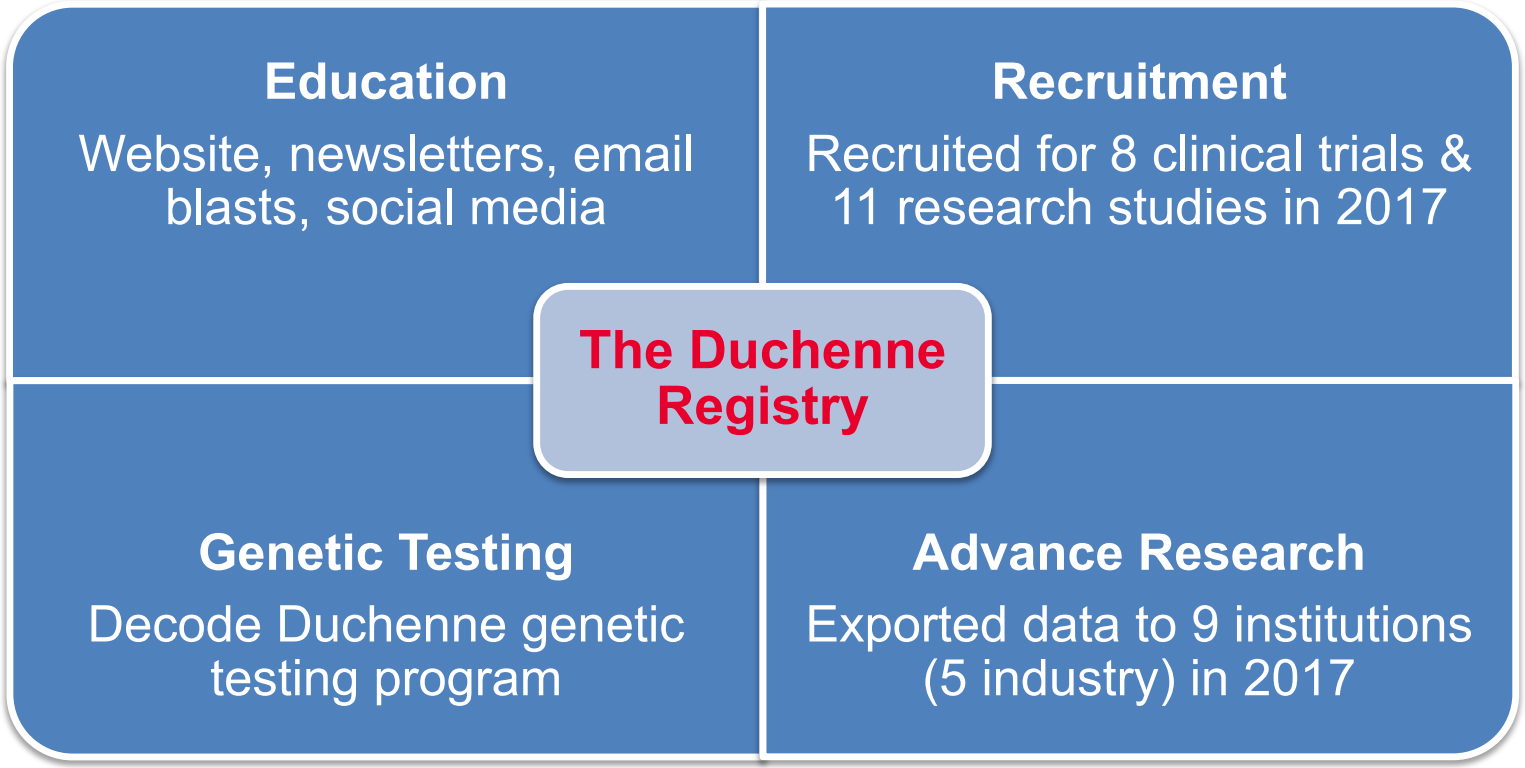
The Duchenne Registry

- Online self-report registry for individuals with Duchenne or Becker, as well as carrier females
- Established by PPMD in 2007, in collaboration with the NIH, CDC and Emory Genetics

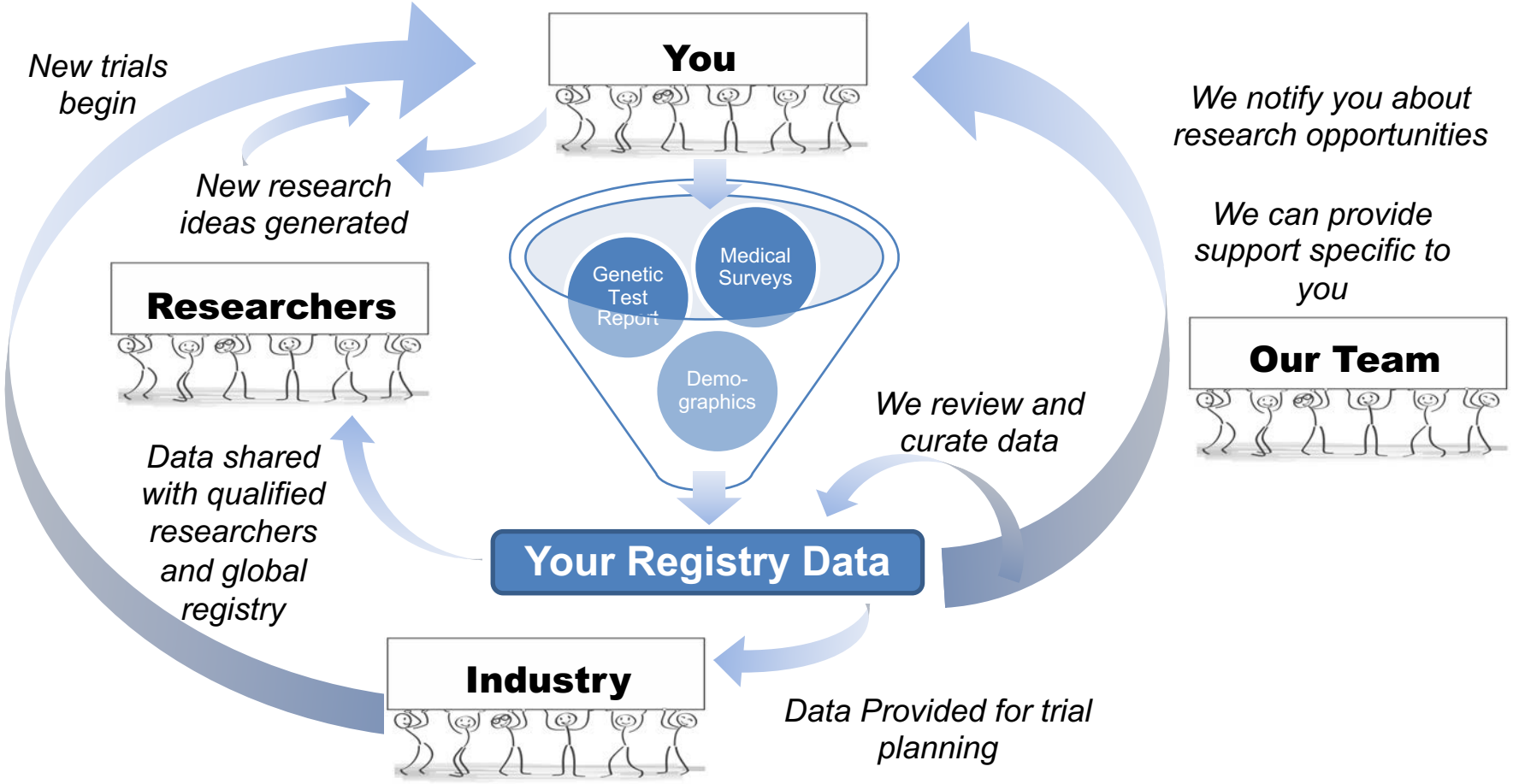
Goal of Duchenne Registry

- To educate and connect the entire Duchenne and Becker community:
  - Individuals with Duchenne and Becker
  - Families and caregivers
  - Healthcare providers
  - Researchers
  - Industry

What We Do


Education
Website, newsletters, email blasts, social media
Recruitment
Recruited for 8 clinical trials & 11 research studies in 2017
The Duchenne Registry
Genetic Testing
Decode Duchenne genetic testing program
Advance Research
Exported data to 9 institutions (5 industry) in 2017

The Duchenne Registry: Working Together to Advance Research



Screenshots from the New Registry Dashboard

THE DUCHENNE REGISTRY

HOME ABOUT REPORTS DASHBOARD VIEW DATA GLOSSARY LOGOUT

Welcome back, Bruce!

Your newest survey, the Corticosteroid Module is now available. Take it today and view the Survey Data to see how others have responded.

CHAT STATUS

Offline

Health Surveys (3 of 12 Complete)

INCOMPLETE SURVEYS

Bone/Orthopedic Module — START SURVEY >

A moderate length survey covering spinal X-rays, scoliosis, bone fractures, ...

Behavior & Learning Module — START SURVEY >

A moderate length survey covering any diagnosed behavior or learning problems ...

Clinical Trials & Registry Participation Module — START SURVEY >

A moderate length survey about your participation in any research studies, ...

Insurance Module — START SURVEY >

Medical Records

Upload relevant medical records to share more detailed data while protecting your privacy.

ADD MEDICAL RECORDS

Medications

Corticosteroid Module

An in-depth survey covering your steroid use including medication, dose, ...

START SURVEY >

Emflaza

An in-depth survey for individuals taking Emflaza. Dose, weight, schedule ...

START SURVEY >

Genetic Testing & Family History Module

A short survey about your genetic test report and your family history. Please ...

START SURVEY >

Your Data at Work

Your data was used in a 2017 publication in the Journal of Neuromuscular Diseases. Learn more.

COMPLETE SURVEYS

Diagnosis Module

Survey completed 04-25-2018 Download results | Update survey

VIEW DATA

Pain Interference - Adults

Survey completed 04-26-2018 Download results | Update survey

VIEW DATA

Healthcare Providers

Add your healthcare providers to help other participants learn which medical professionals see people with the same condition.

ADD PROVIDER

Growth Measurements

Easily track your height and weight

ADD MEASUREMENTS

Family Members

Your Data at Work

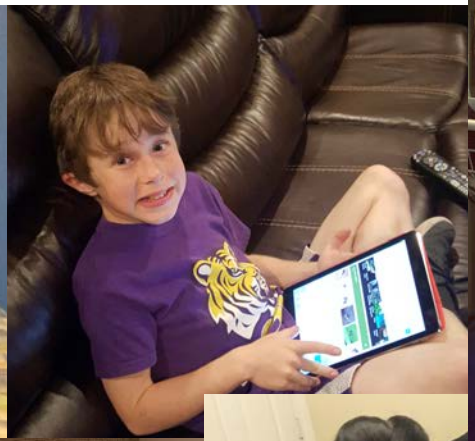
Your de-identified data is shared with:

- TREAT-NMD Global Duchenne Registry
- Duchenne Regulatory Science Consortium

Your Data Makes a Difference
Register Today!

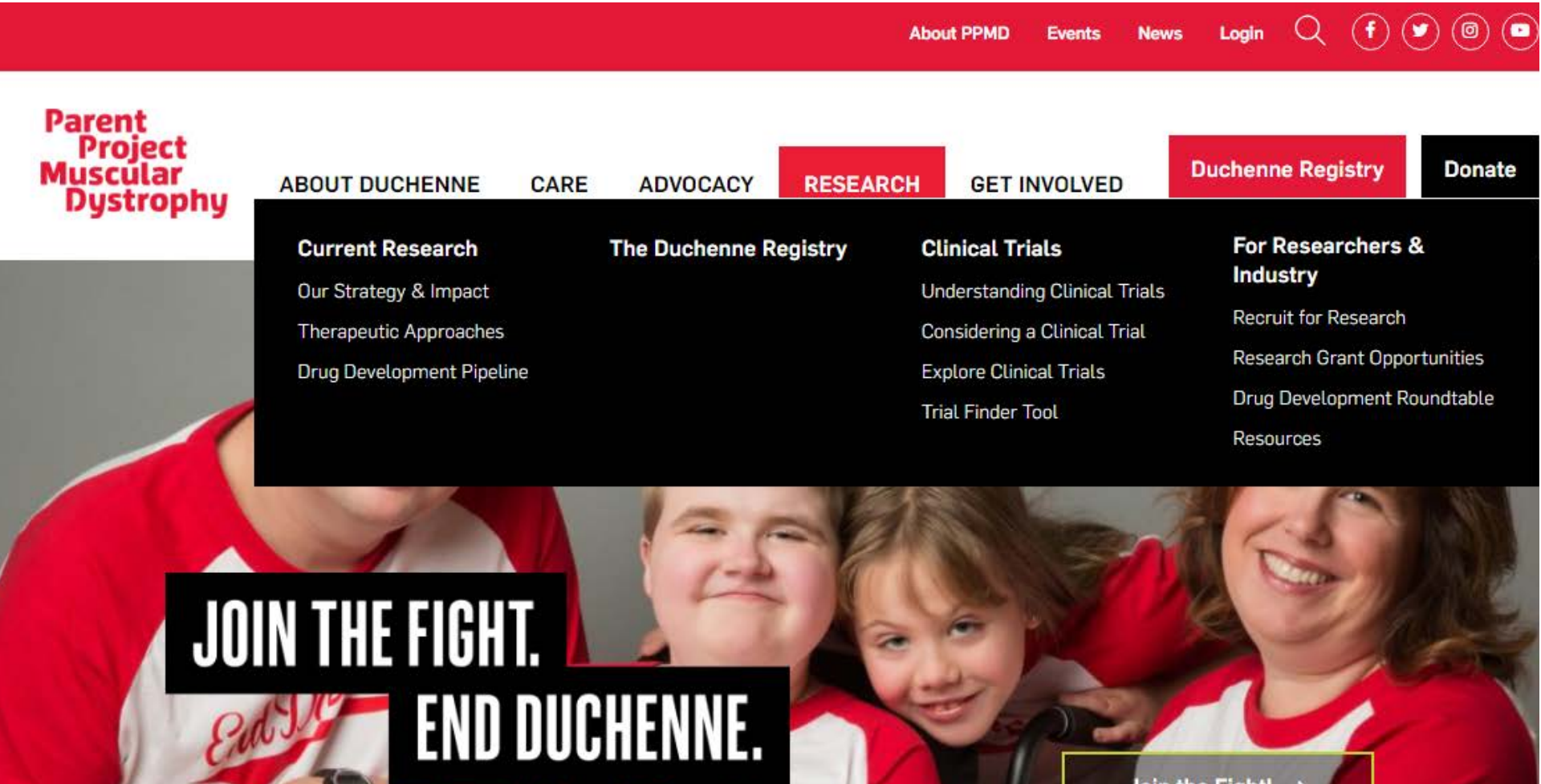
www.duchenneregistry.org

You Could Win an iPad!



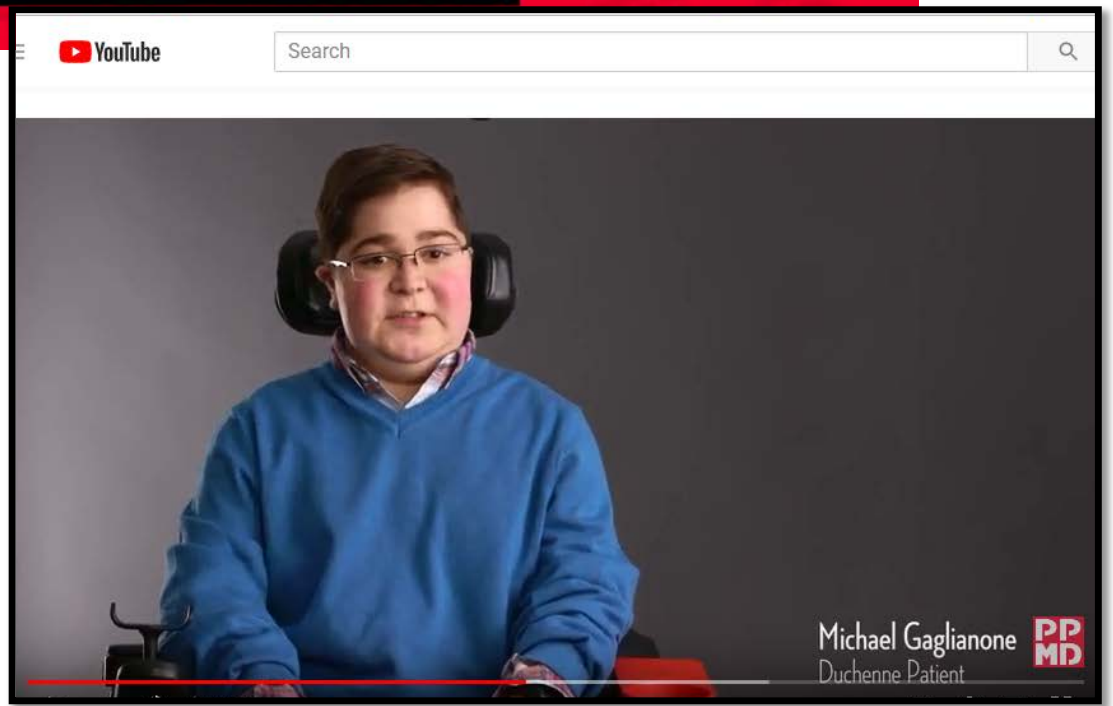
PP MD

Research > Clinical Trials



UNDERSTANDING CLINICAL TRIALS

CLINICAL TRIAL VIDEO LIBRARY



CLINICAL TRIALS

CONSIDERING A CLINICAL TRIAL

MAKING THE RIGHT CHOICE ABOUT CLINICAL TRIALS

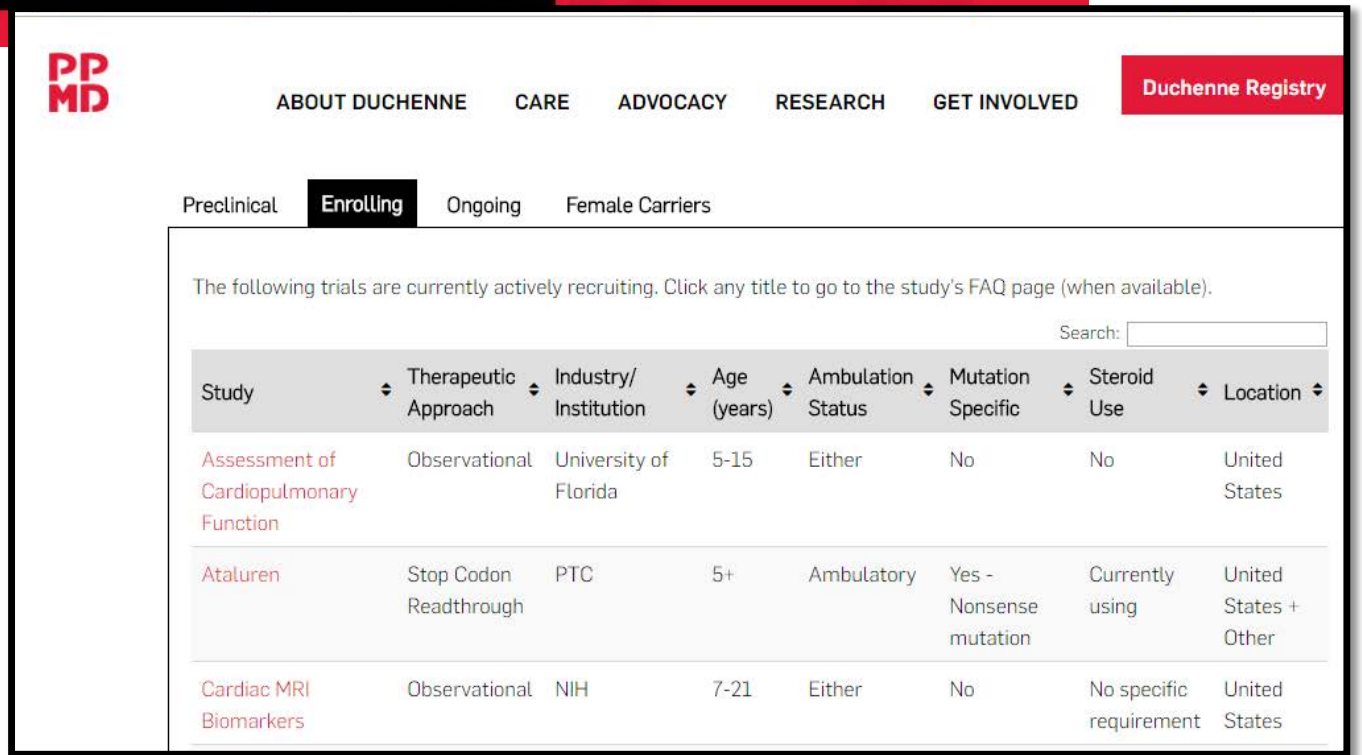
A Guide for Adults with Duchenne and Becker Muscular Dystrophy

Parent Project Muscular Dystrophy
LEADING THE FIGHT TO END DUCHENNE

RTI INTERNATIONAL

CLINICAL TRIALS

EXPLORE CLINICAL TRIALS



PPMD

ABOUT DUCHENNE CARE ADVOCACY RESEARCH GET INVOLVED Duchenne Registry

Preclinical | Enrolling | Ongoing | Female Carriers

The following trials are currently actively recruiting. Click any title to go to the study's FAQ page (when available).

Search:

Study	Therapeutic Approach	Industry/ Institution	Age (years)	Ambulation Status	Mutation Specific	Steroid Use	Location
Assessment of Cardiopulmonary Function	Observational	University of Florida	5-15	Either	No	No	United States
Ataluren	Stop Codon Readthrough	PTC	5+	Ambulatory	Yes - Nonsense mutation	Currently using	United States + Other
Cardiac MRI Biomarkers	Observational	NIH	7-21	Either	No	No specific requirement	United States

Thank you!

Please visit us at the Registry table!

coordinator@duchenneregistry.org

888-520-8675