ABC's of *RYR1*-related Diseases

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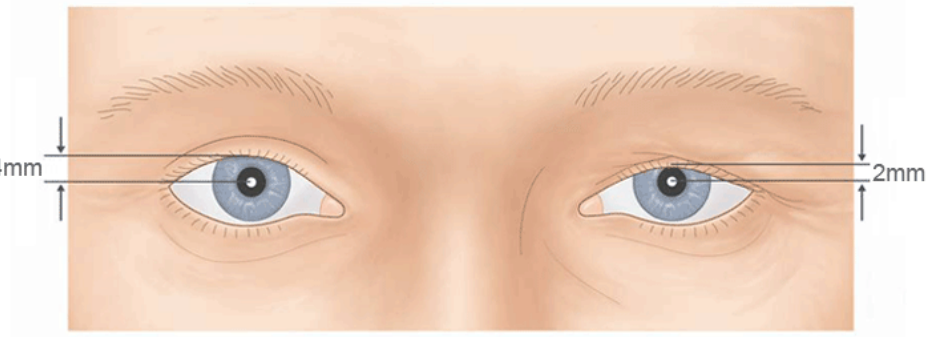
Outline

- Diagnostic Process
  - Symptoms
  - EMG/NCV
  - Muscle MRI/ultrasound
  - Muscle Biopsy
  - Contracture Testing for MH
  - Genetic Testing
- Inheritance Patterns
- Genotype-Phenotype Correlations

Symptoms

- Long face
- Ptosis (drooping eye lids)
- Ophthlamoplegia (restricted movements of the eye muscles)

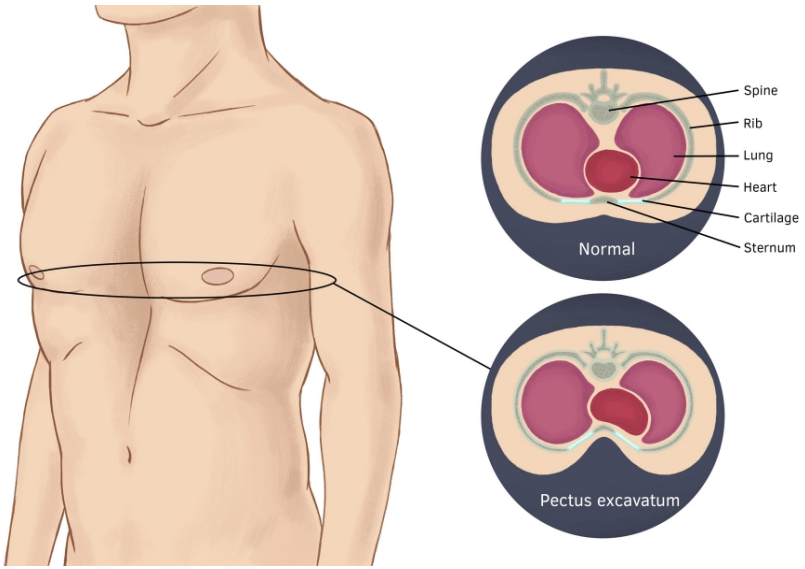


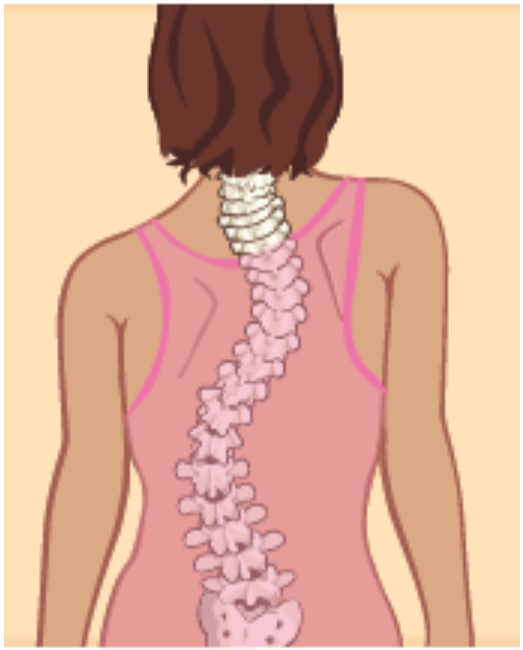
Symptoms (cont.)

- Muscle weakness
  - Facial and proximal (muscles closest to the core) muscles
  - Delays in sitting, walking, etc
  - Difficulties getting up off the floor/out of a chair
  - Difficulties walking
  - Difficulties with stairs
- Muscle wasting (muscles get smaller)
- Muscle cramping/pain
- Rhabdomyolysis (severe breakdown of muscle tissue, muscle cramping/pain/weakness, dark urine, high CK)
- Susceptibility to malignant hyperthermia (MH)

Symptoms (cont.)

- Contractures (fixed/stiff joints)
- Scoliosis (spine curvature)
- Changes in the shape of the chest
- Hip dislocation

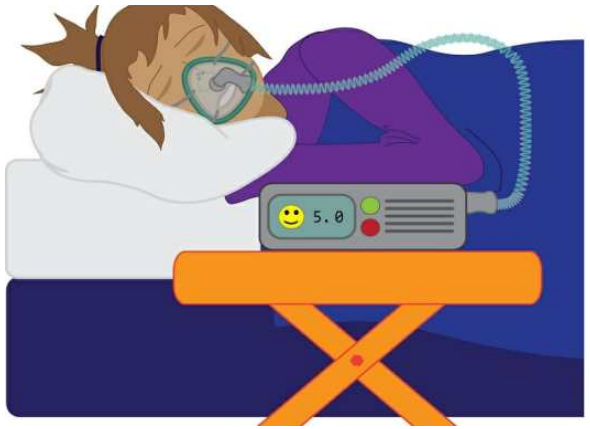




Scoliosis

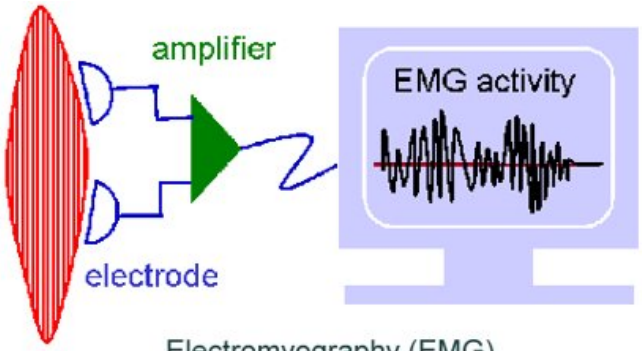
Symptoms (cont.)

- Eating difficulties
- Breathing difficulties, sleep apnea (difficulties breathing during sleep)
- Fatigue (especially in warm weather), exercise intolerance
- Intelligence is typically normal



EMG/NCV

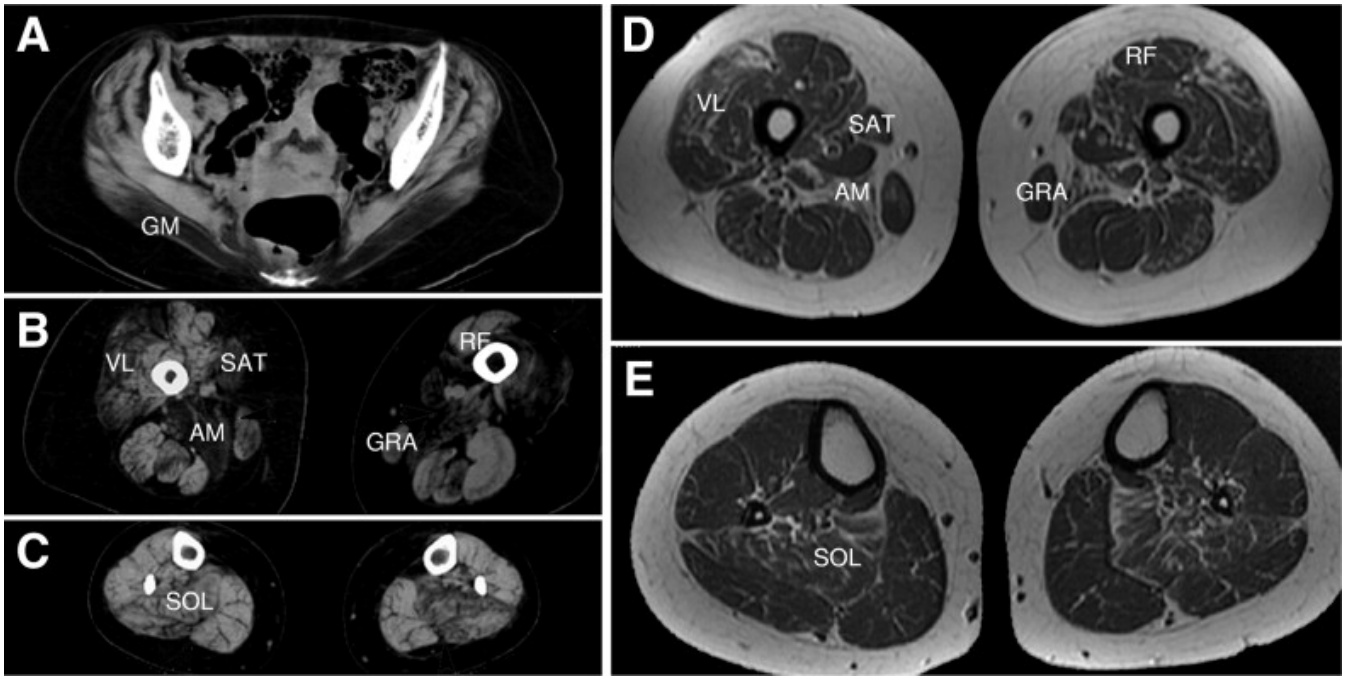
- Electromyography (EMG)
  - Assesses the muscle activity
  - Needle (recording microphone)
- Nerve conduction velocities (NCV)
  - Assesses the nerve signals
  - Recording electrodes placed over the nerves



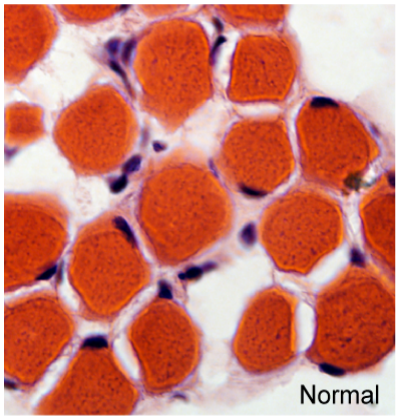
Electromyography (EMG)

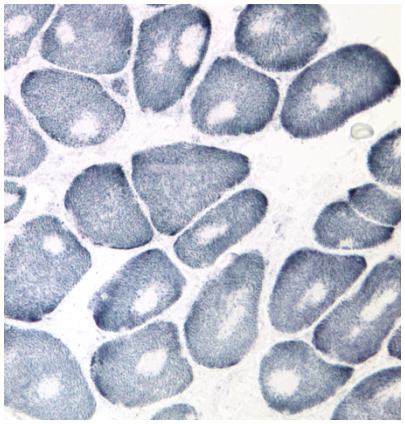
Muscle MRI & Ultrasound

- Looks for patterns of muscle groups that are affected

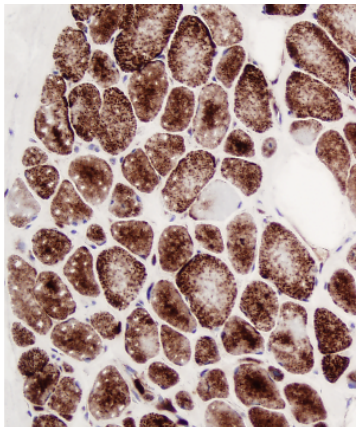


Biopsy Findings of *RYR1*-related Myopathies

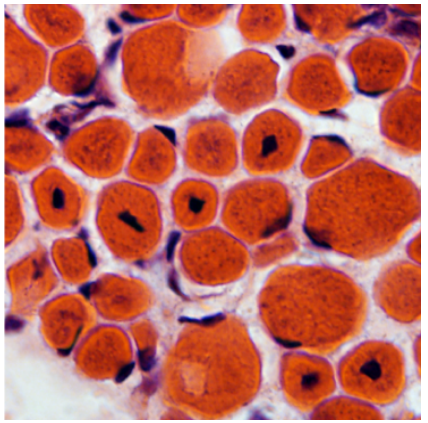




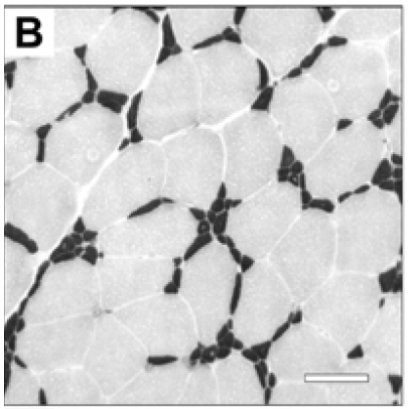
Central Core Disease (CCD)



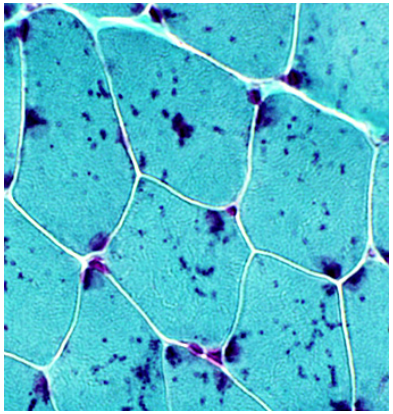
Multiminicore Disease (MmD)



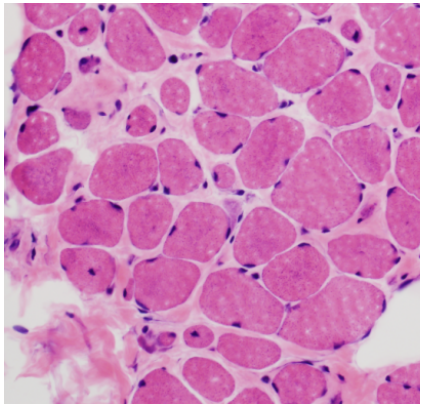
Centronuclear Myopathy (CNM)



Congenital Fiber Type Disproportion (CFTD)

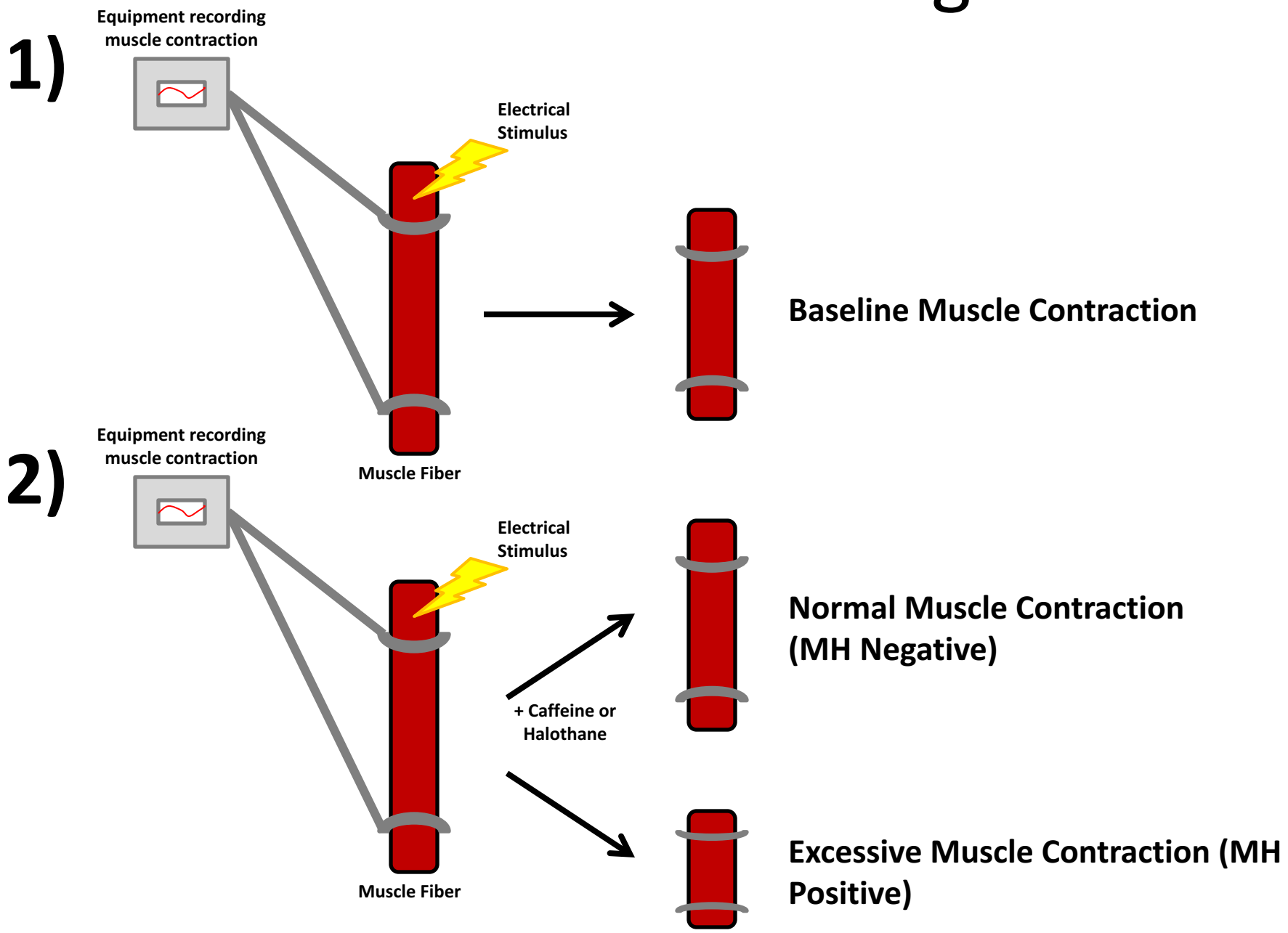


Nemaline Myopathy (NM)



Congenital Muscular Dystrophy (CMD)

Contracture Testing

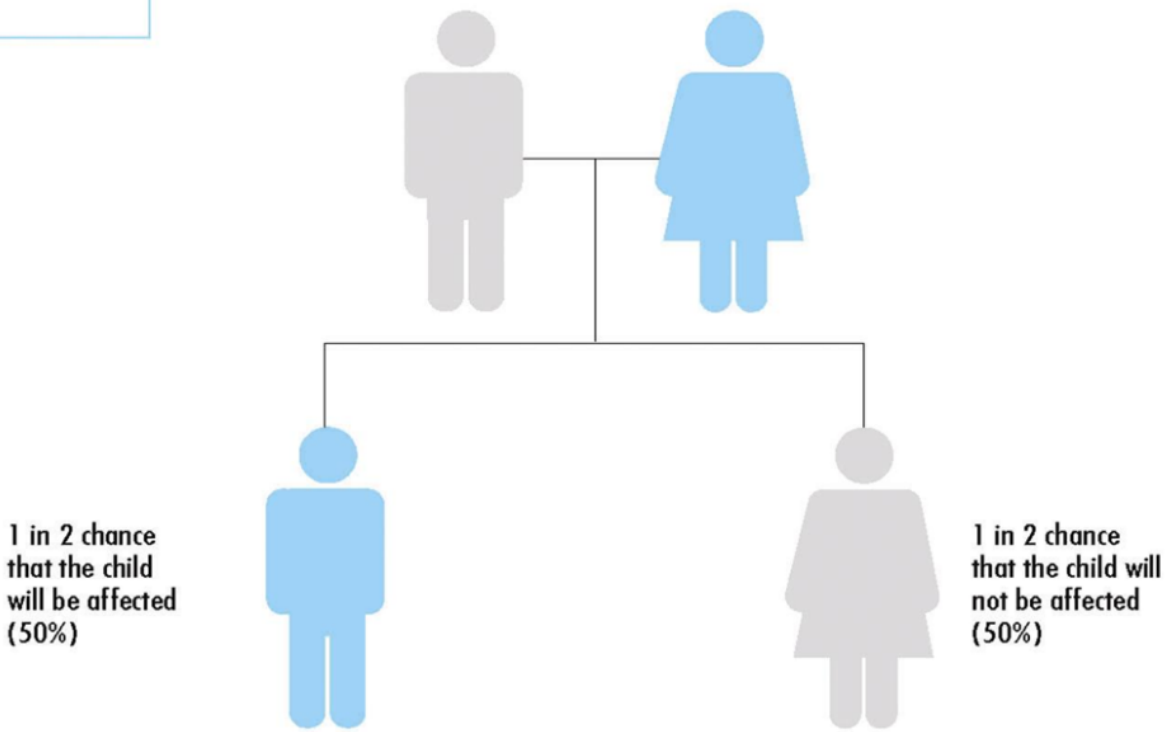


Genetic Testing

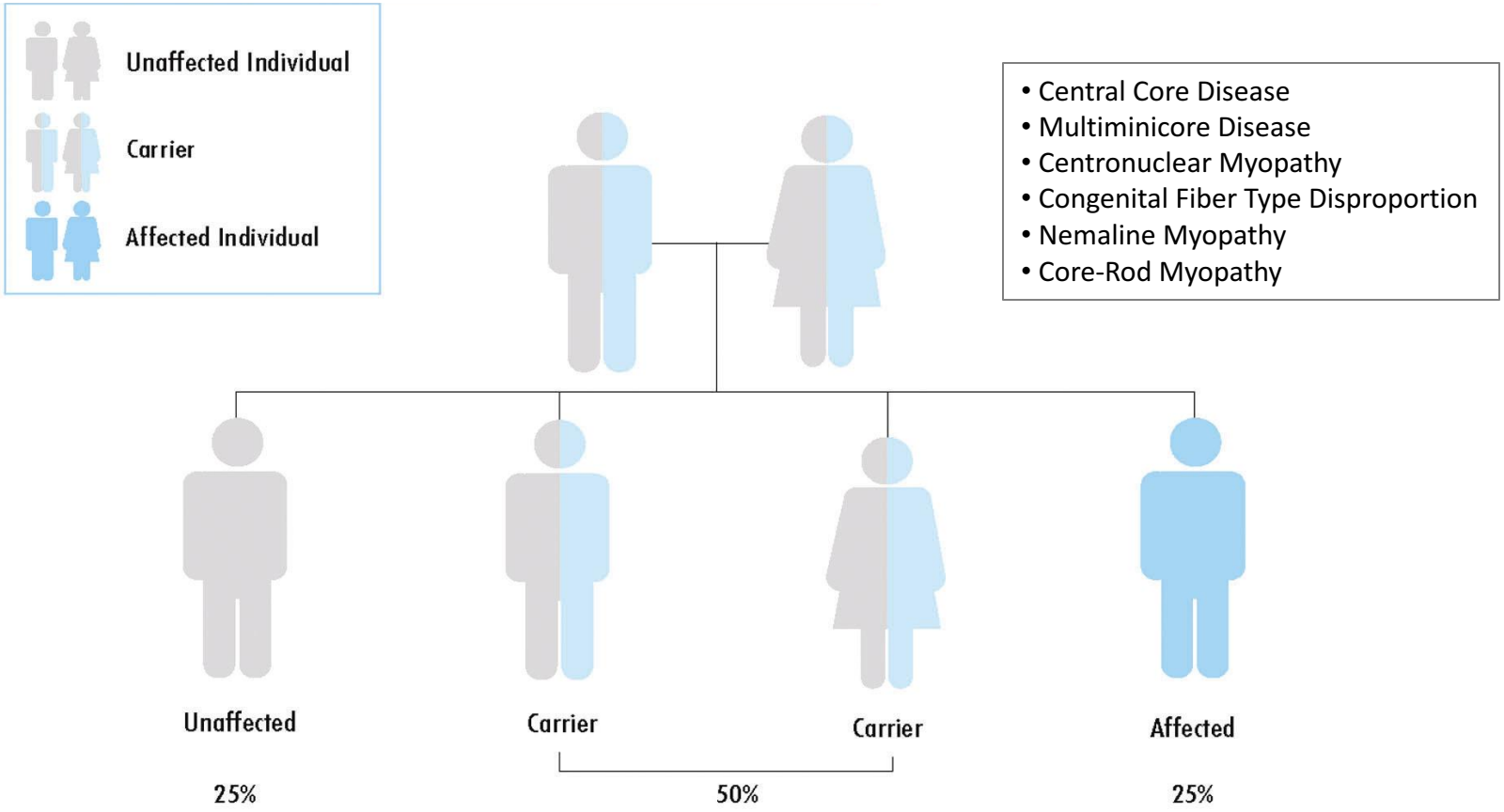
- Options:
  - Sequencing
  - Deletion/Duplication
  - Panel
  - Whole exome/genome sequencing
- Interpretation of Results
  - Medical Literature
  - Prediction Programs
  - Prevalence of the Change

Autosomal Dominant Inheritance

- Central Core Disease
- Core-Rod Myopathy



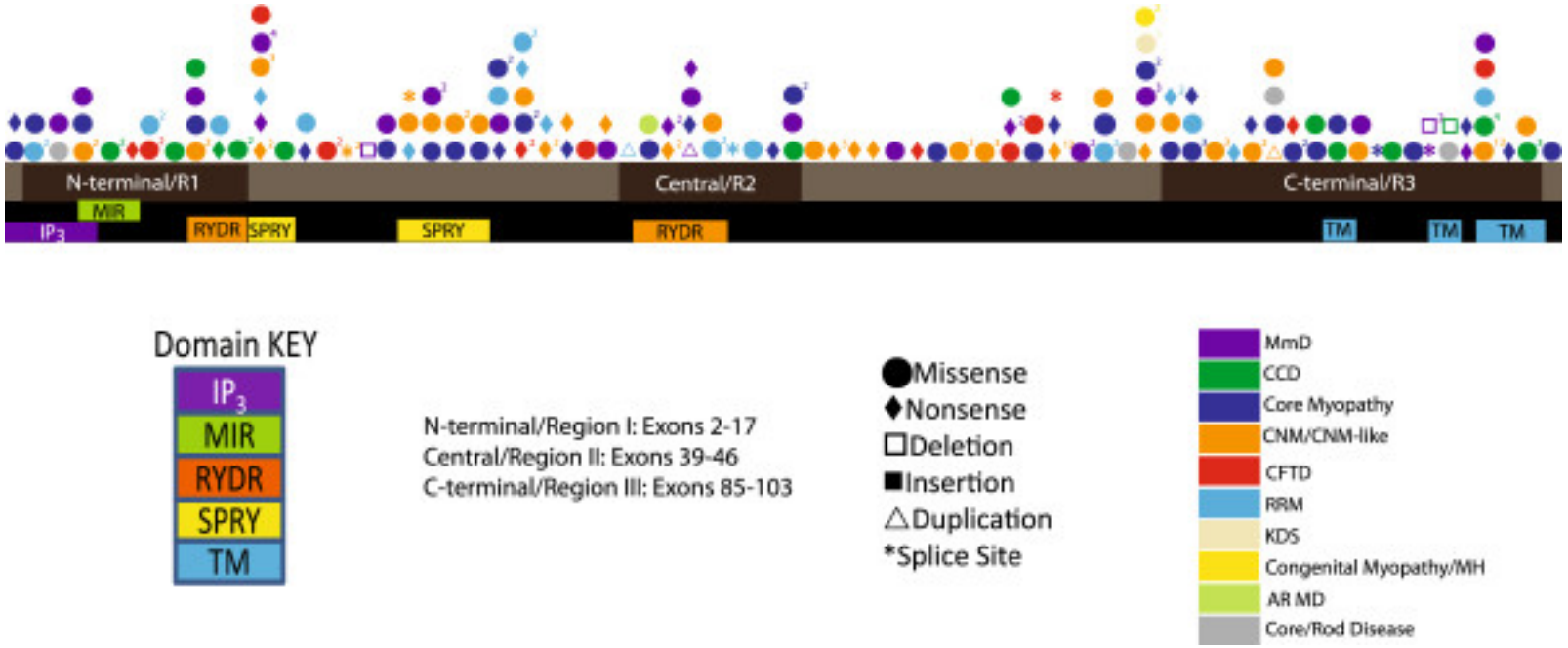
Autosomal Recessive Inheritance



- Central Core Disease
- Multiminicore Disease
- Centronuclear Myopathy
- Congenital Fiber Type Disproportion
- Nemaline Myopathy
- Core-Rod Myopathy

Genotype-Phenotype Correlations

- Location and type of the gene change
- Affect on protein levels



Core-Rod Myopathy

Core Myopathy

King Denborough Syndrome

Nemaline Myopathy

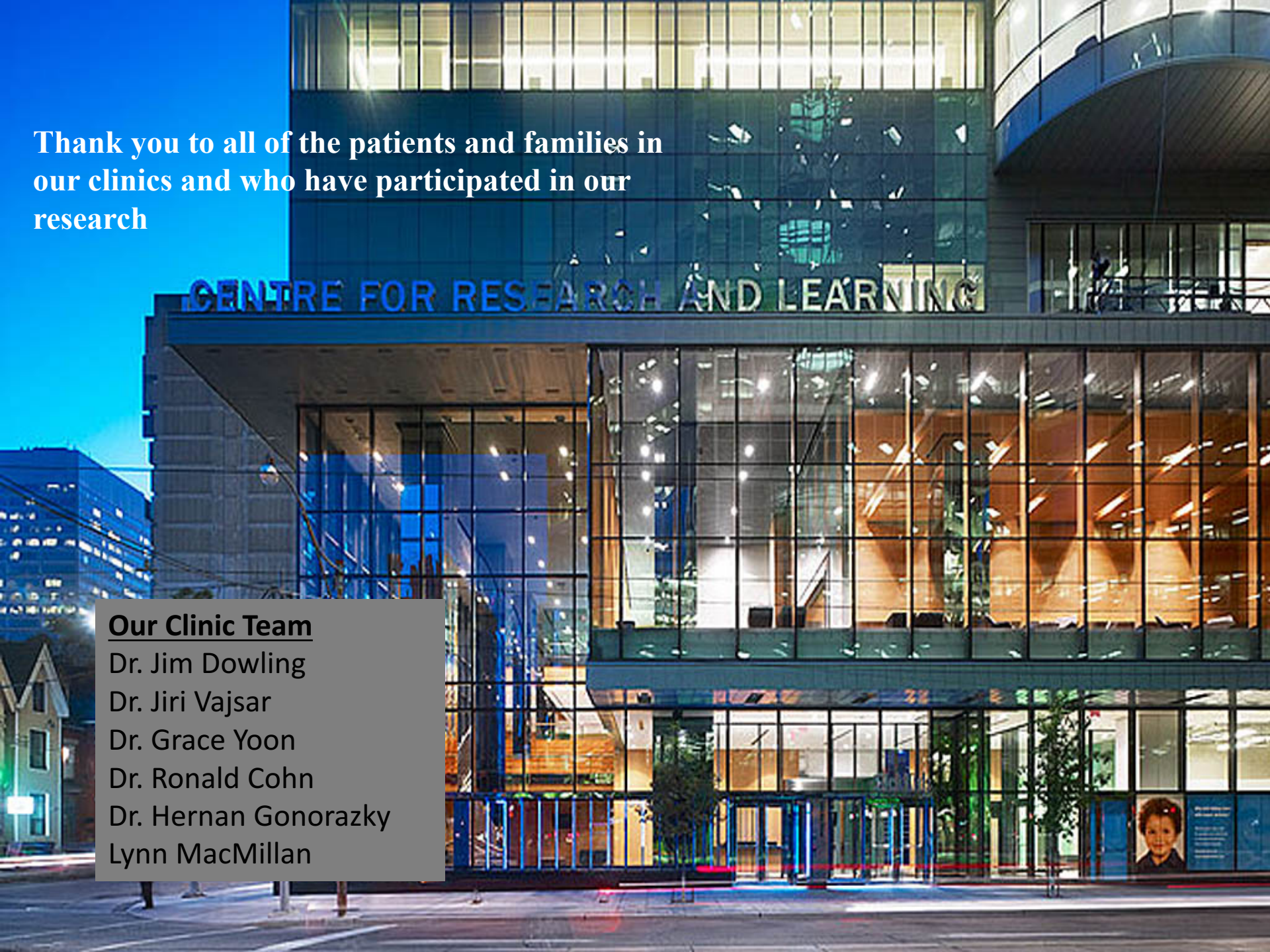
RYR1-Related Myopathy

Congenital Muscular Dystrophy

Multimincore Disease

Centronuclear Myopathy

Central Core Disease



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Our Clinic Team

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