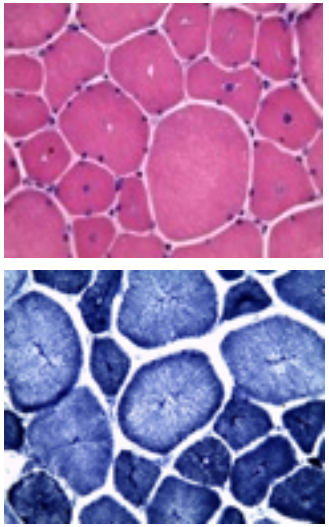
A few words about DNM2

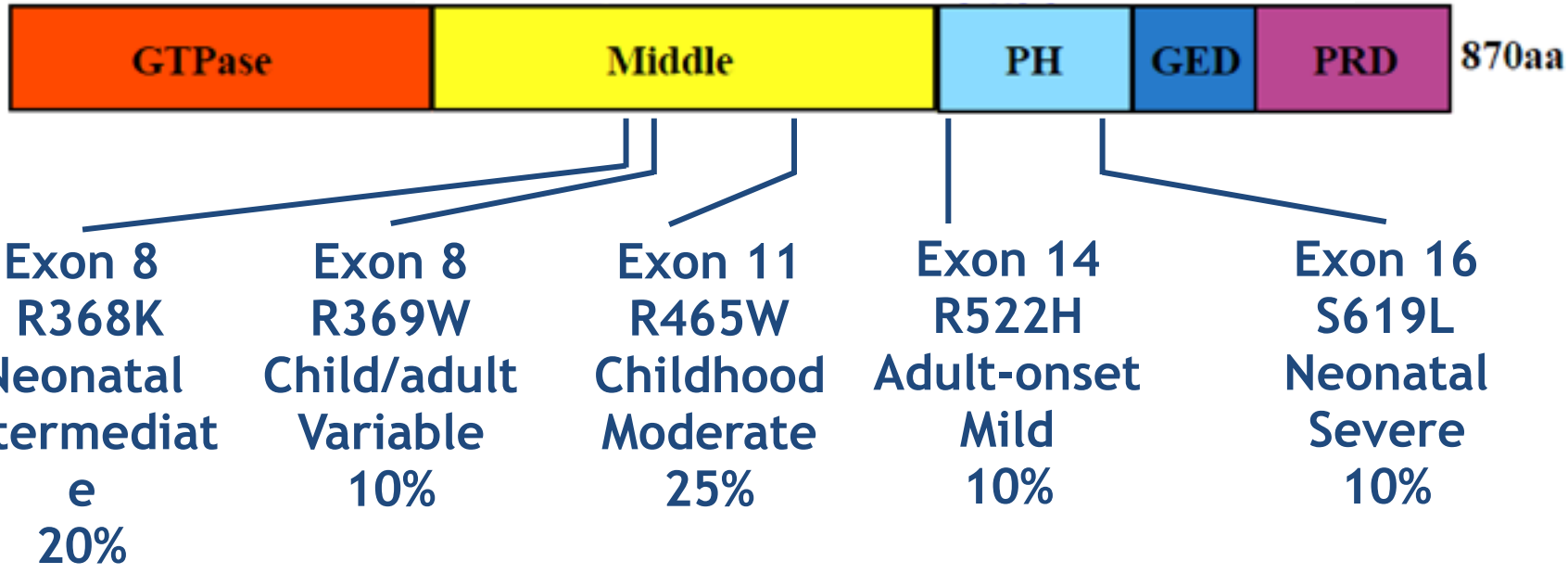
Clinics, histology, genetics



> 100 families described (MTM1: 500, BIN1: 15)

Histology: fiber size variability, spoke of wheels

Genetics: Mutation "Hotspots"
→ prognosis possible



Nuclei during muscle development

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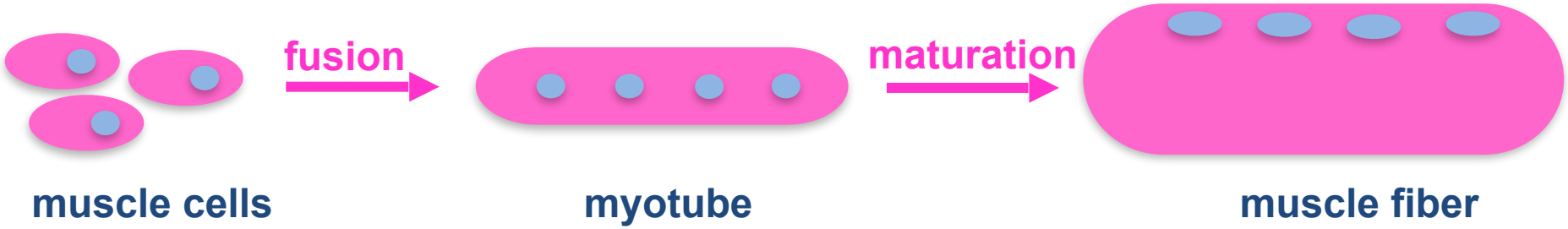

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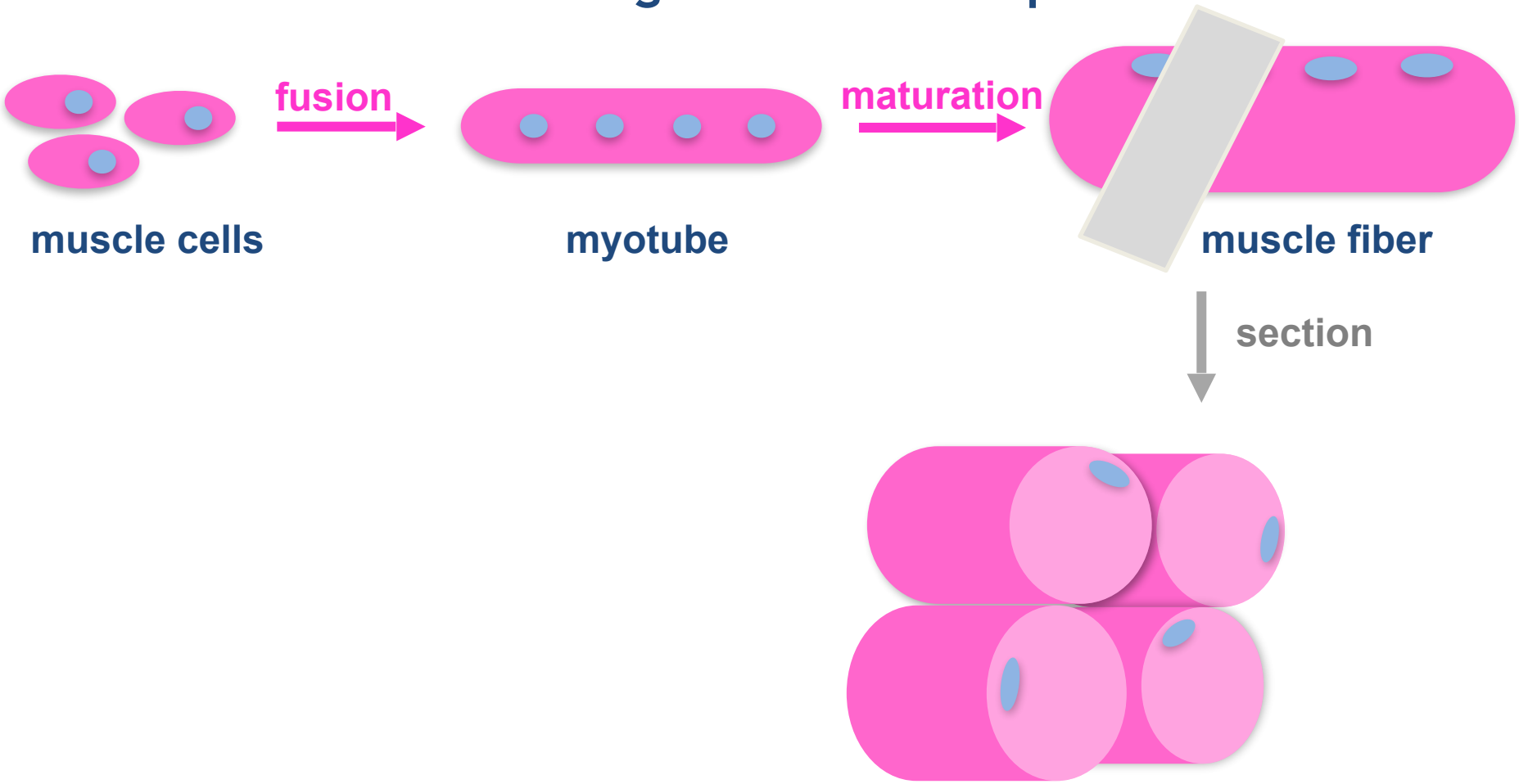

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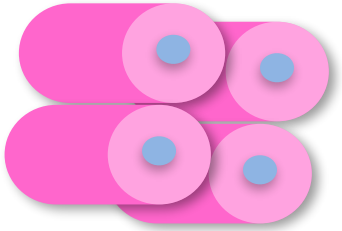
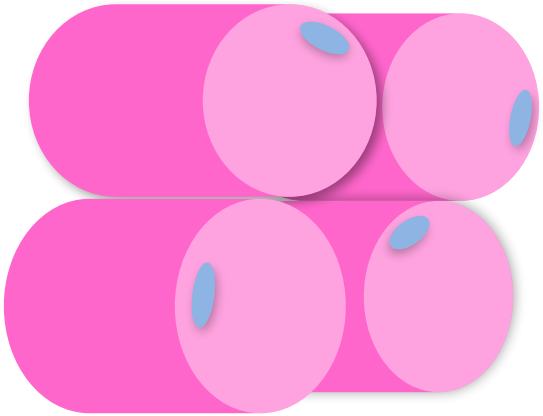
section





“myotubular myopathy”

muscle fibers look like myotubes before maturation

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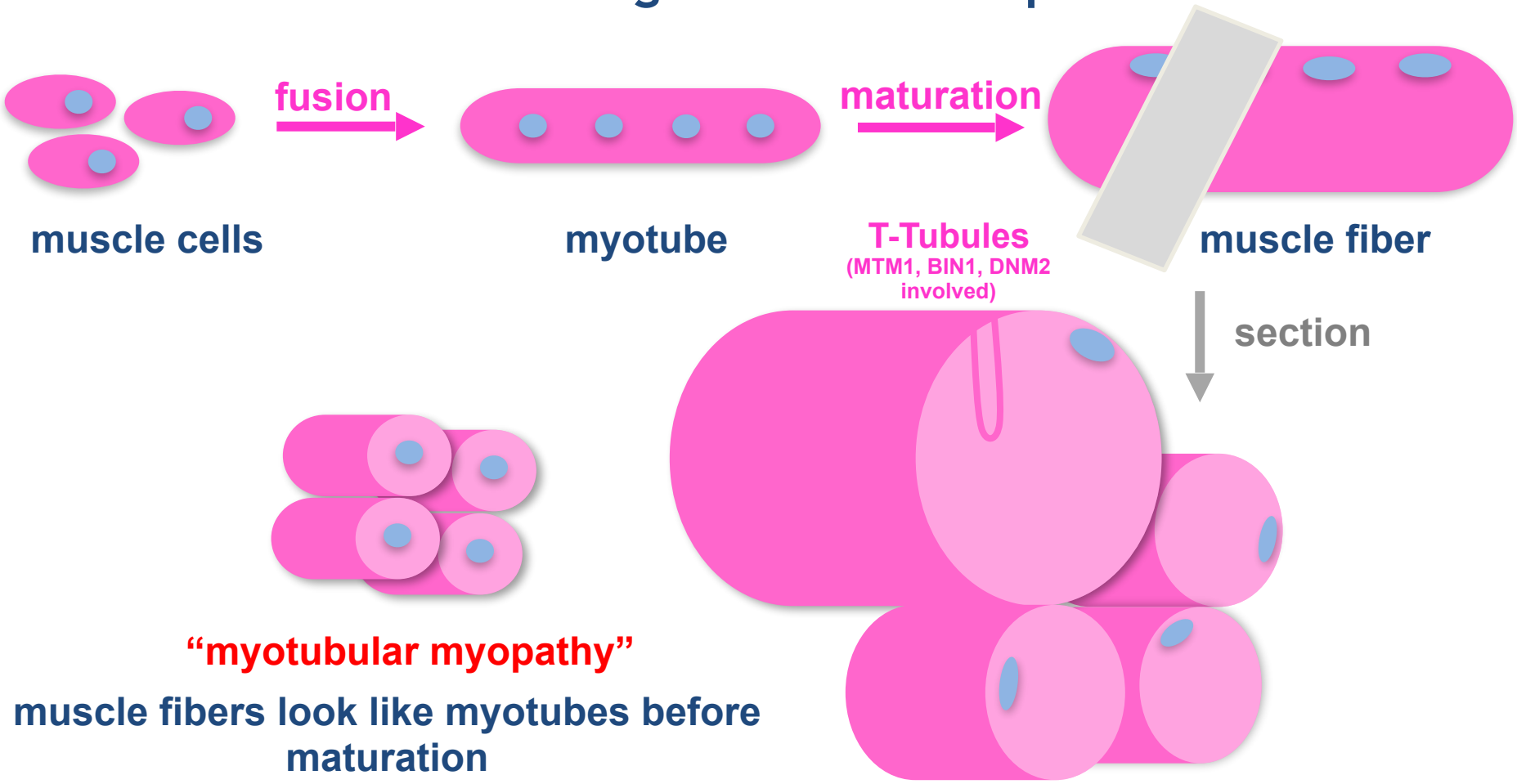

MTM1, BIN1, DNM2, RYR1, TTN involved in muscle structure

Structure determines function

Nuclei during muscle development

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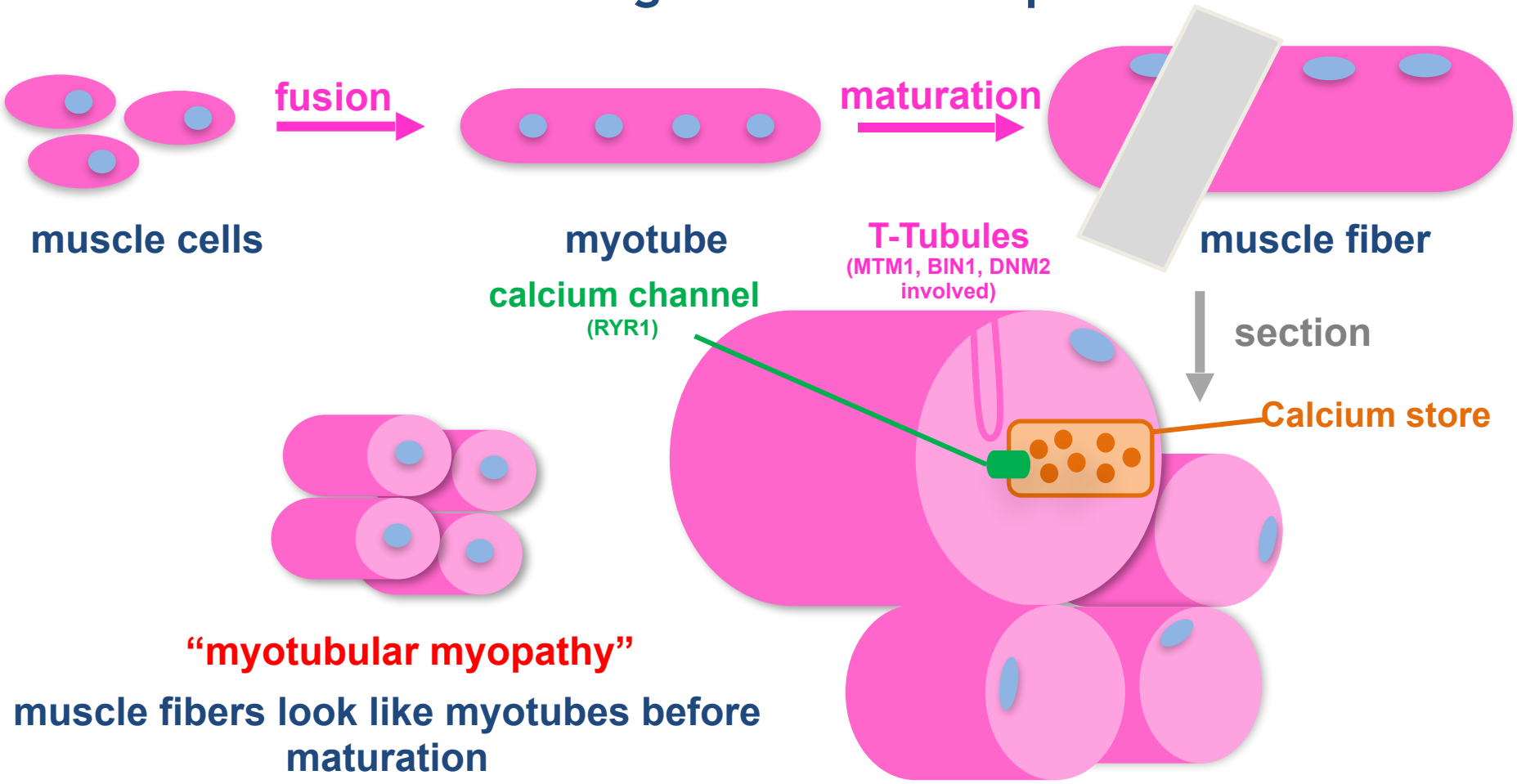

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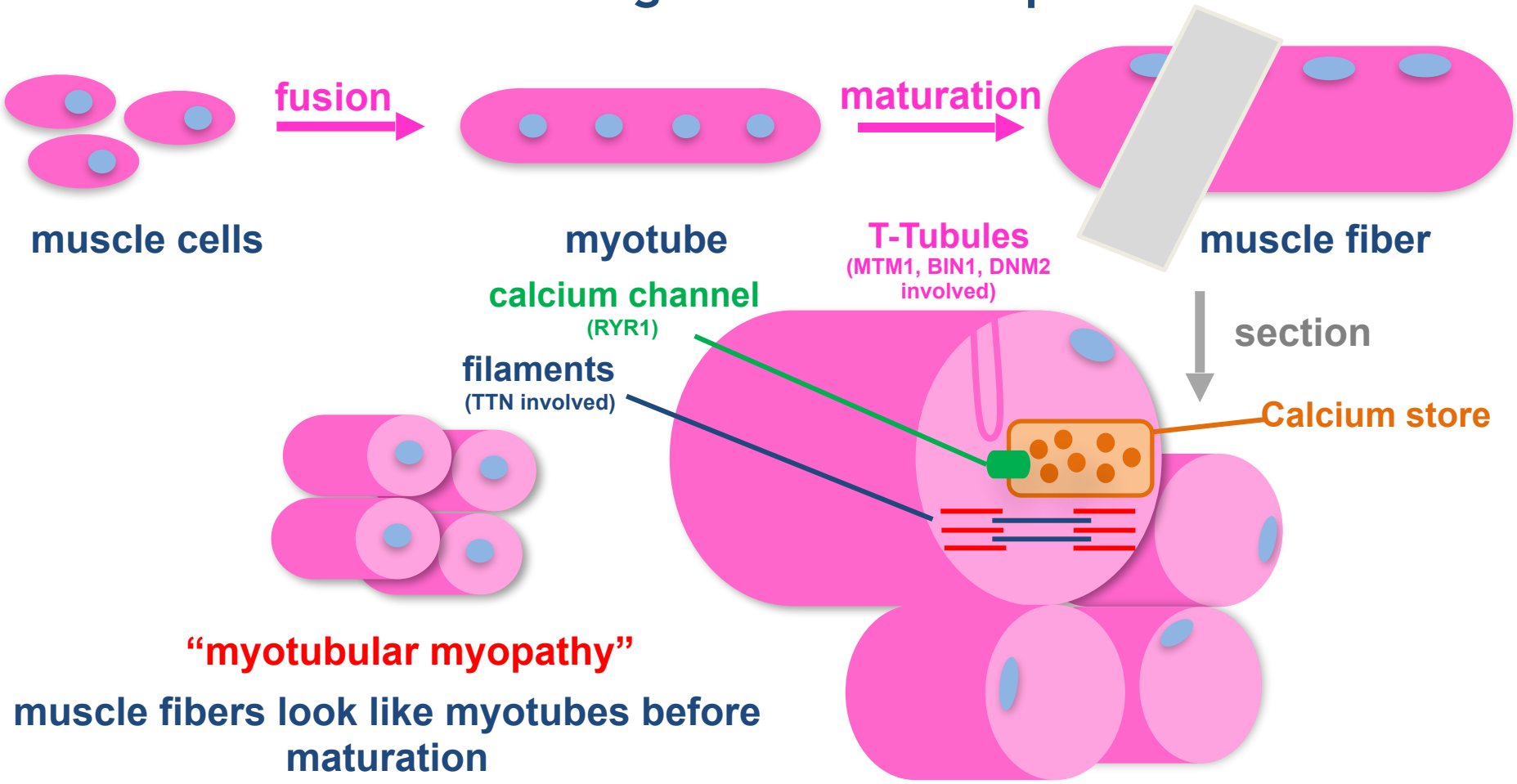

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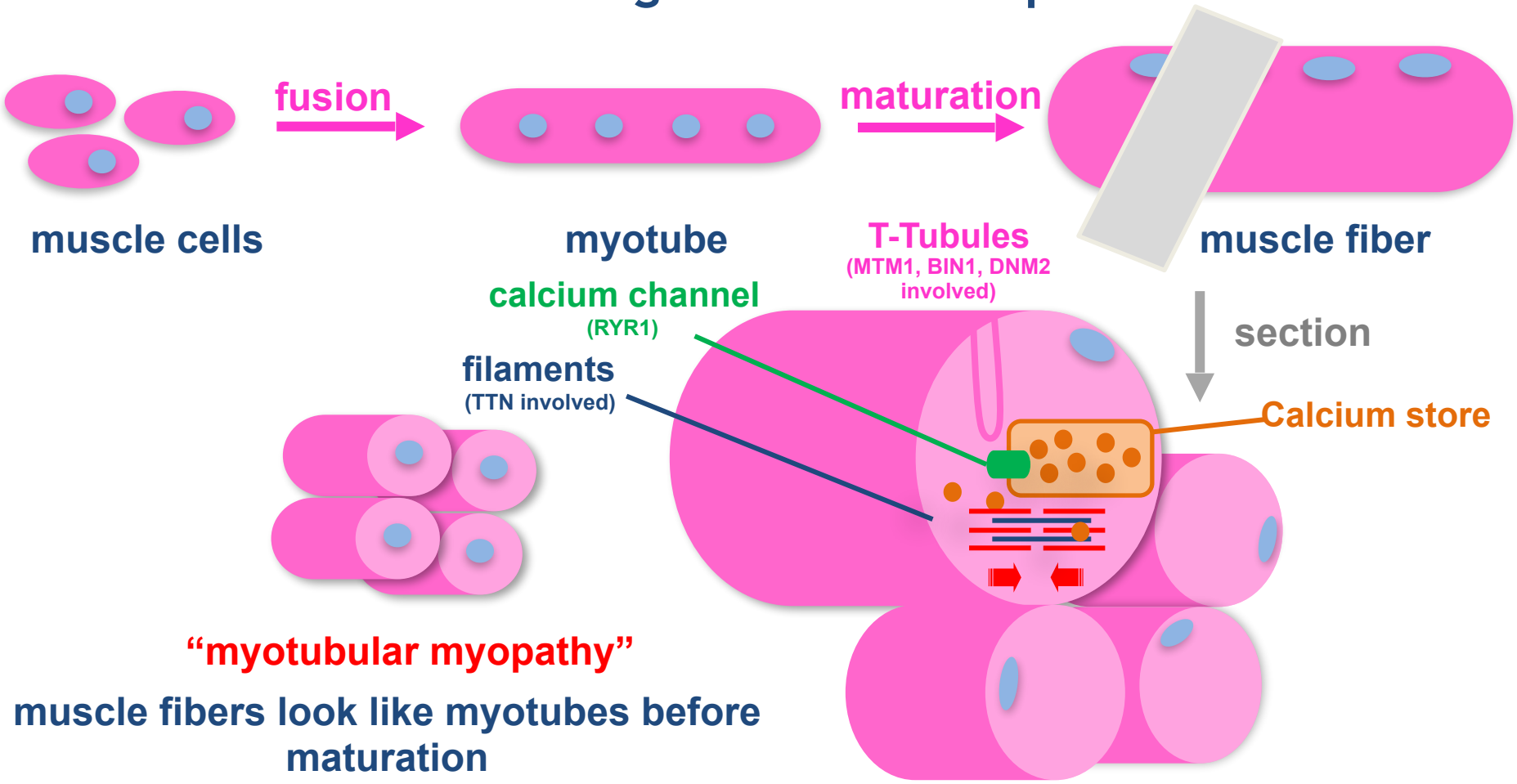

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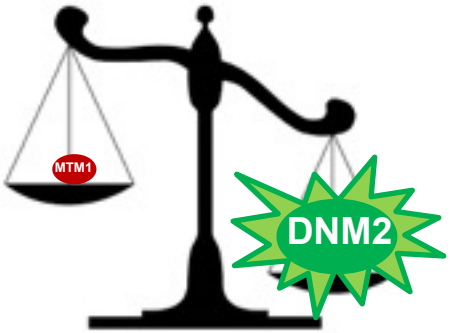
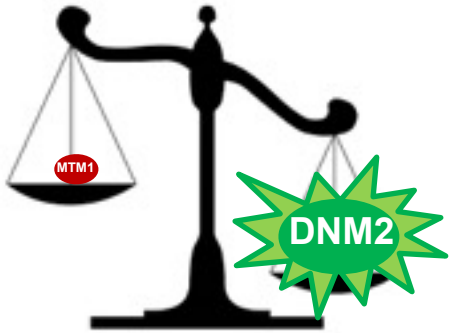
Structure determines function

Cross therapy
Idea and applications



Myotubular myopathy:
MTM1/DNM2 imbalance in muscle

Cross therapy
Idea and applications



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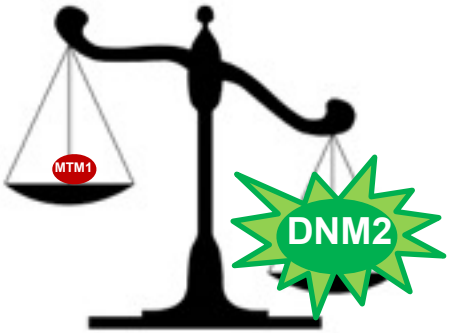
→ **Reduction of DNM 2 as therapy?**

Cross therapy
Idea and applications



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Mice without MTM1 and less DNM2:
normal life span + almost normal force

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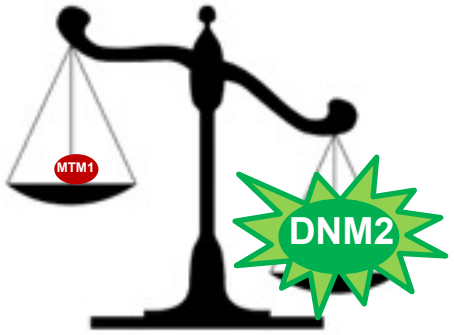

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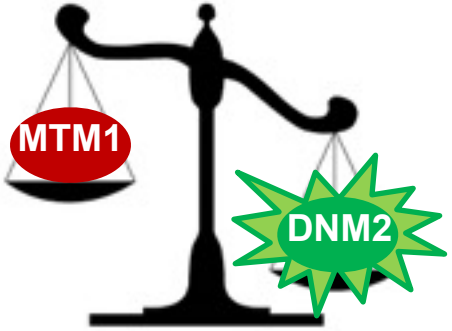
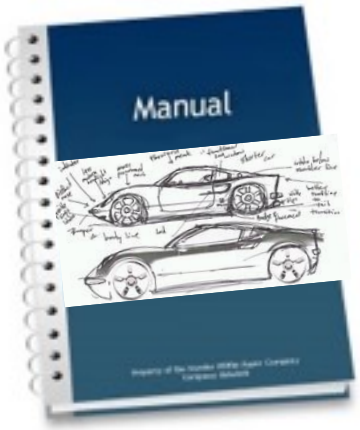


Centronuclear myopathy:
Similar MTM1/DNM2 imbalance in muscle

Same therapeutic approach for MTM / CNM?

How could we reduce DNM2 in patients?

In mice we removed DNM2 genetically



A gene is a fragment of a chromosome
It carries the information for a protein

DNM2 is like a manual to build a car

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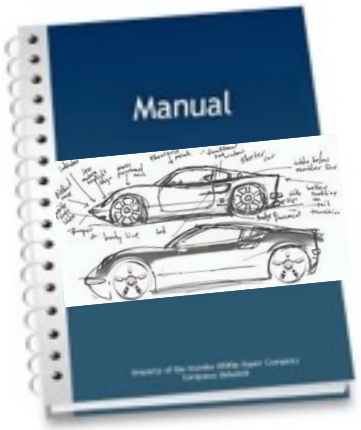

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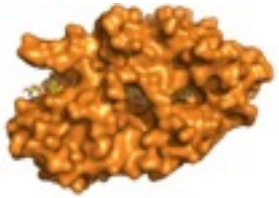

A protein has an activity in the cell

Dynamin 2 is the car

Two possibilities to reduce DNM2

1. At the DNA level: produce less dynamin

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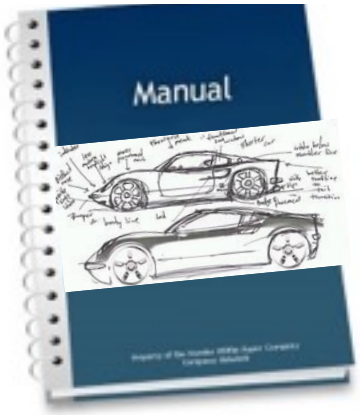

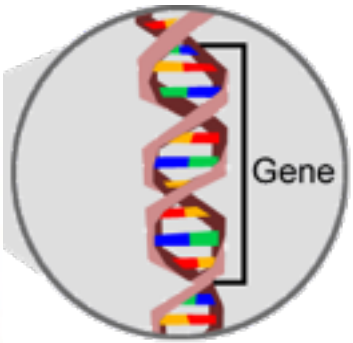

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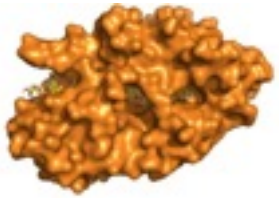

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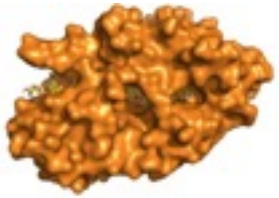

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Two possibilities to reduce DNM2

1. At the DNA level: produce less dynamin 2
2. At the protein level: block dynamin 2