

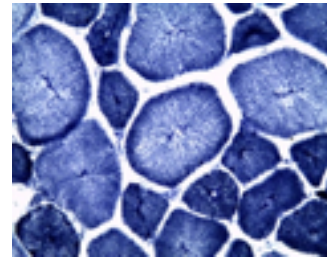
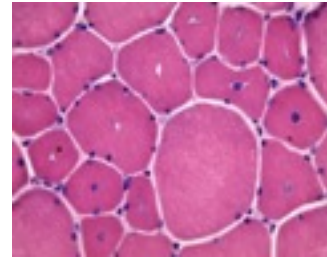
# A few words about DNM2

Clinics, histology, genetics

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

**Histology:** fiber size variability, spoke of wheels

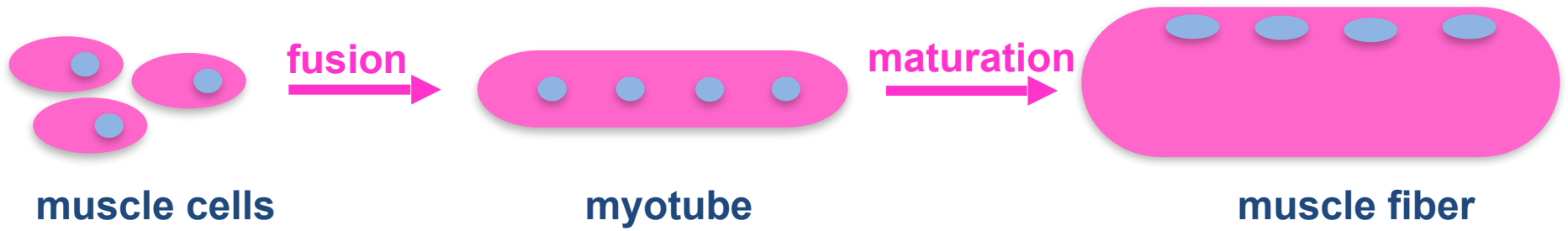
**Genetics:** Mutation “Hotspots”  
→ prognosis possible



Exon 8 R368K Neonatal Intermediate 20%	Exon 8 R369W Child/adult Variable 10%	Exon 11 R465W Childhood Moderate 25%	Exon 14 R522H Adult-onset Mild 10%	Exon 16 S619L Neonatal Severe 10%
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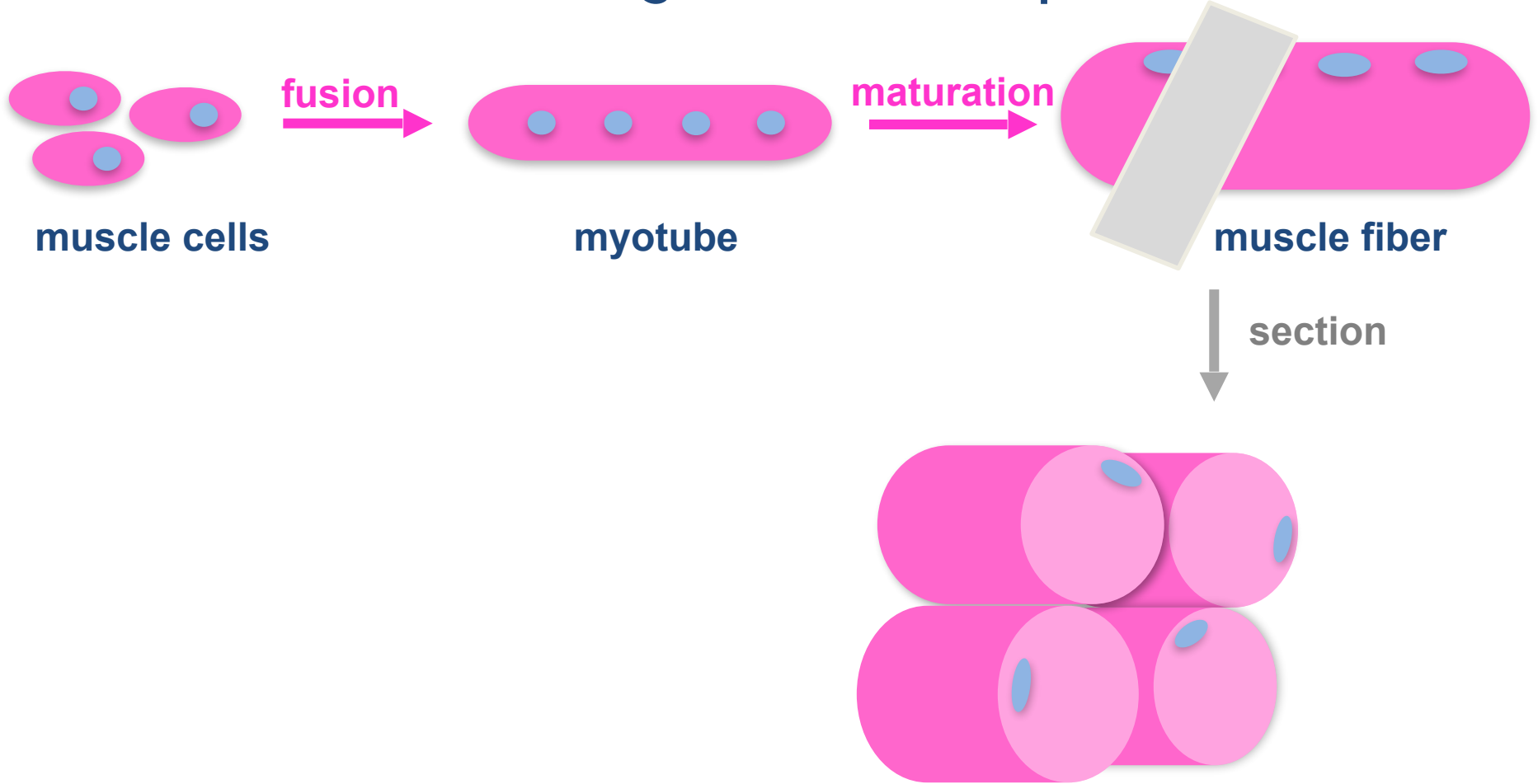
# Nuclei during muscle development

## Nuclei during muscle development



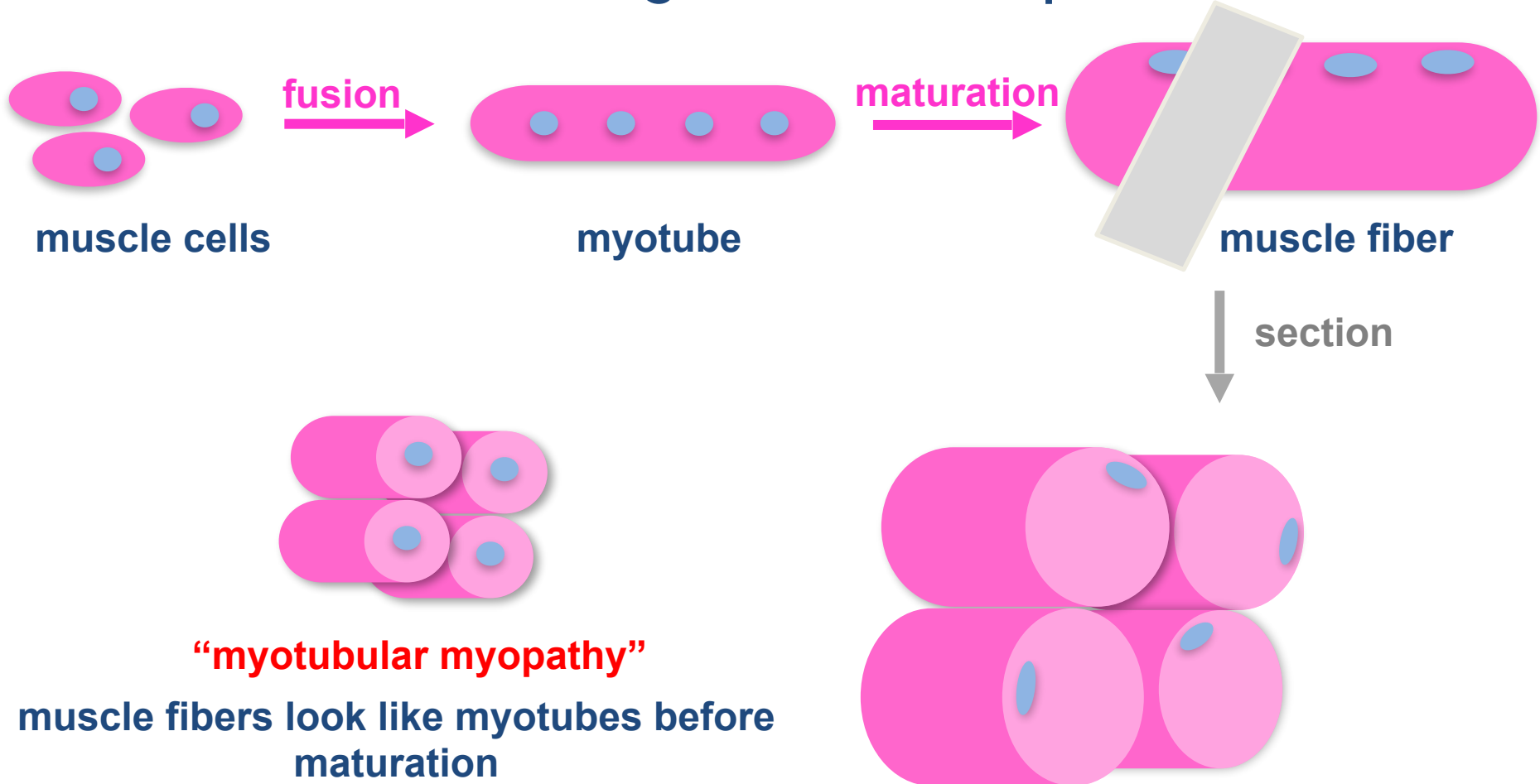
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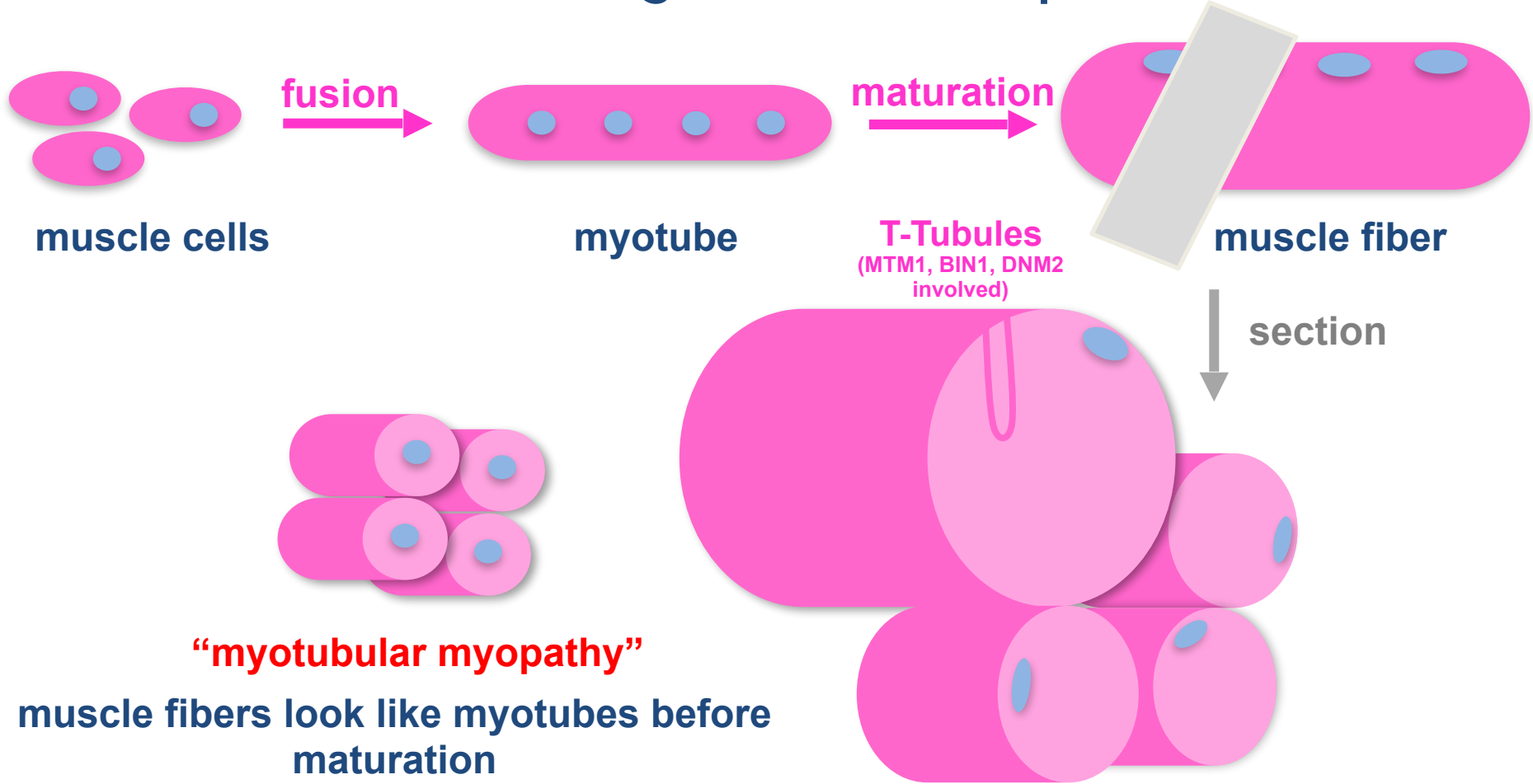
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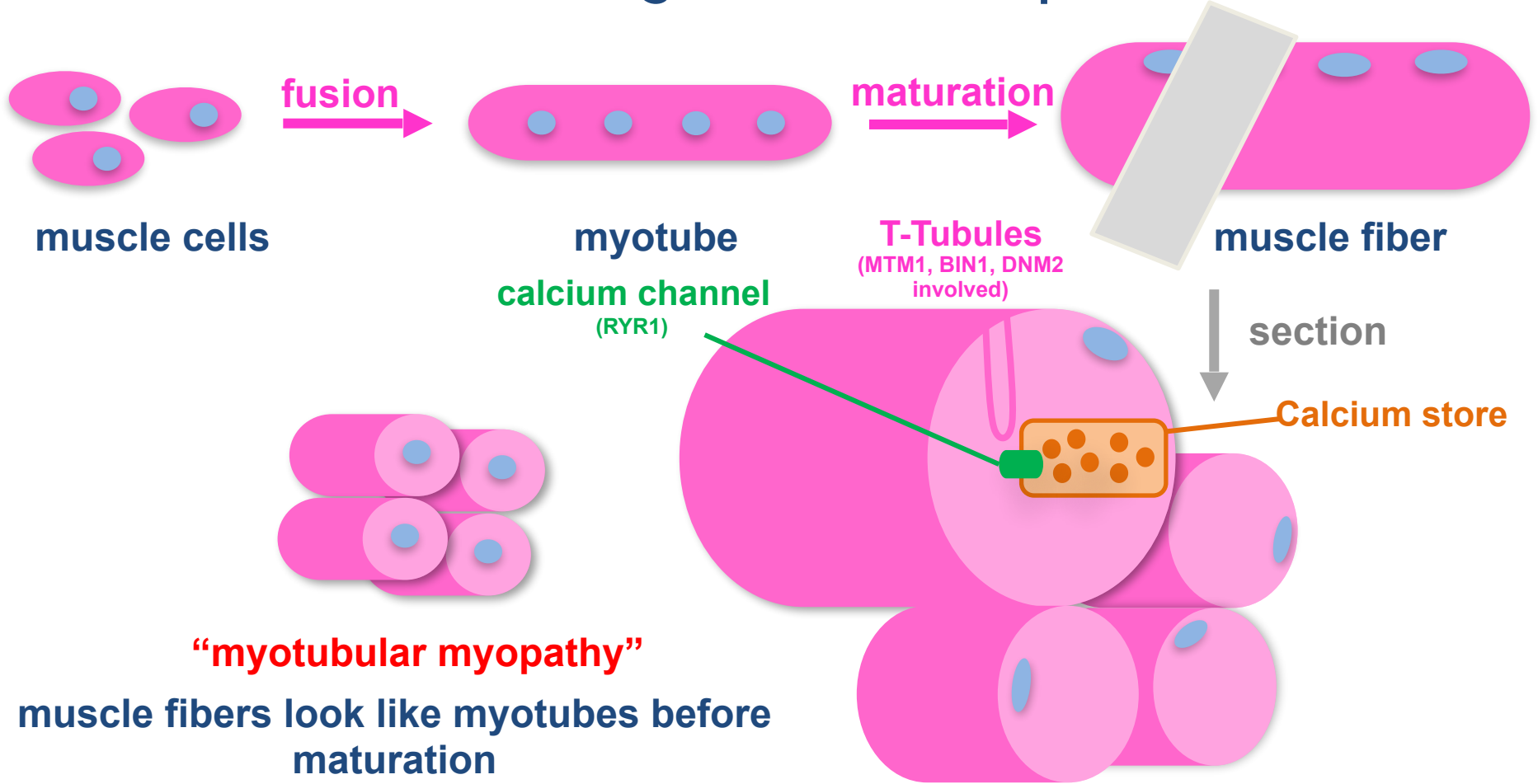


MTM1, BIN1, DNM2, RYR1, TTN involved in muscle structure

**Structure determines function**

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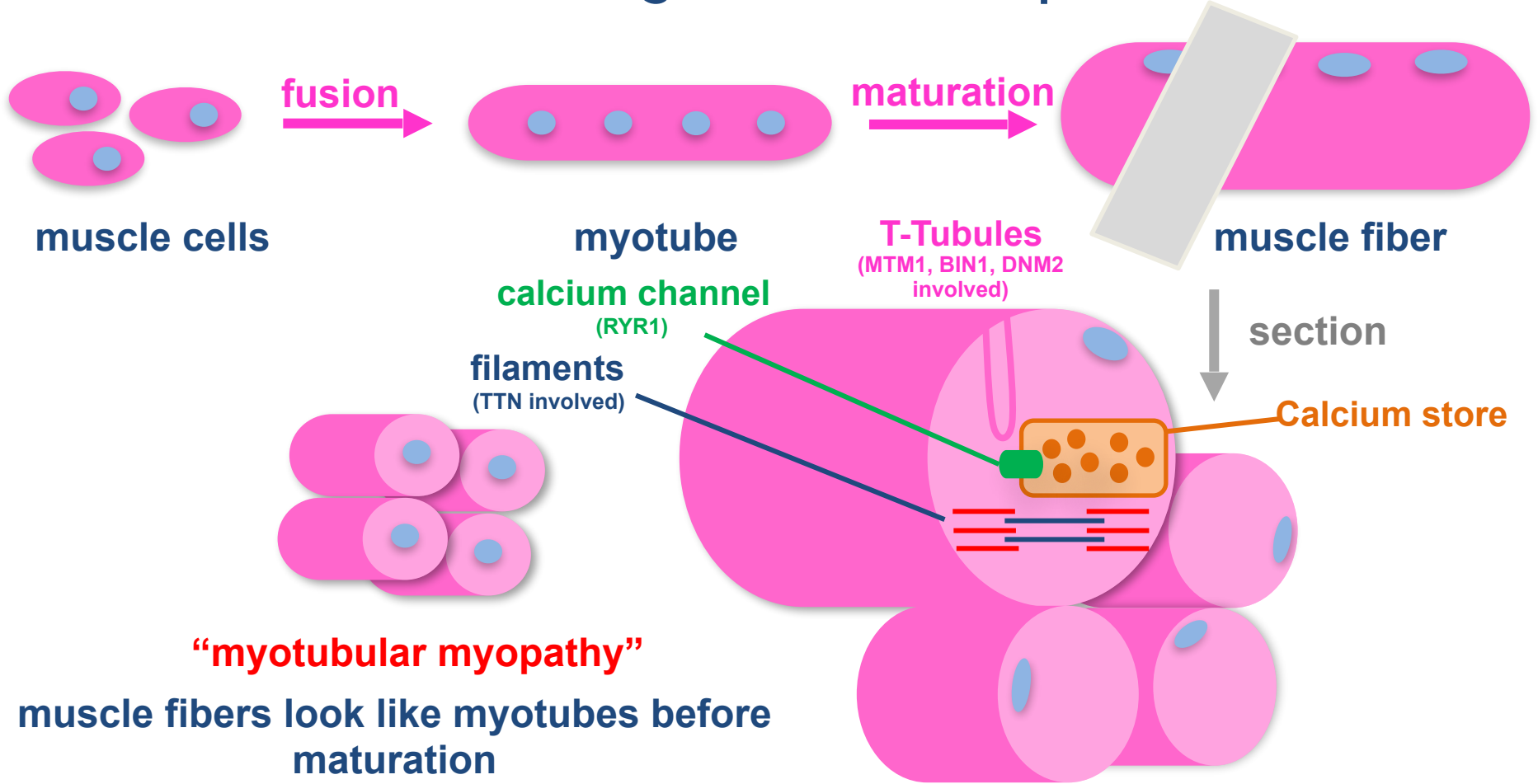


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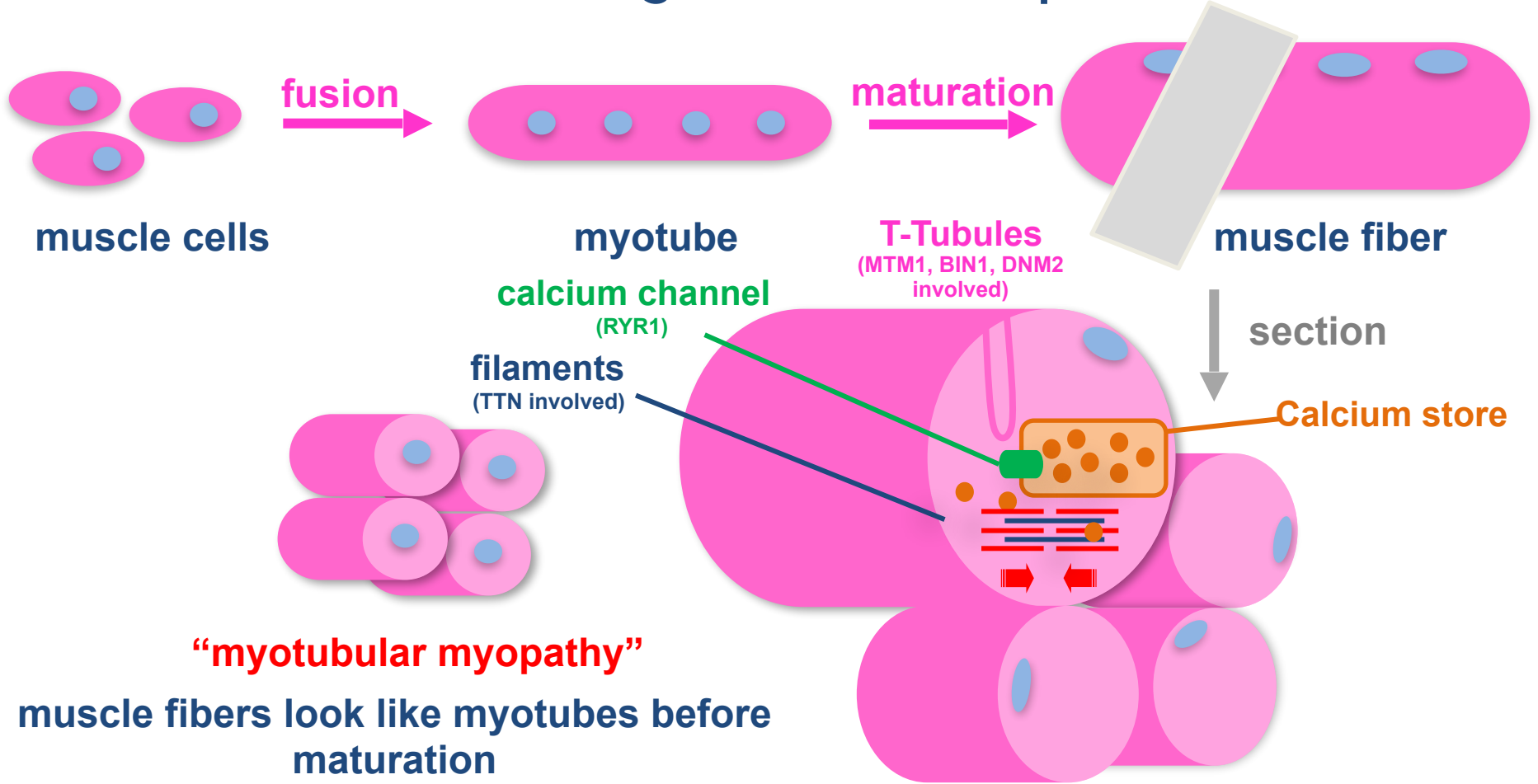


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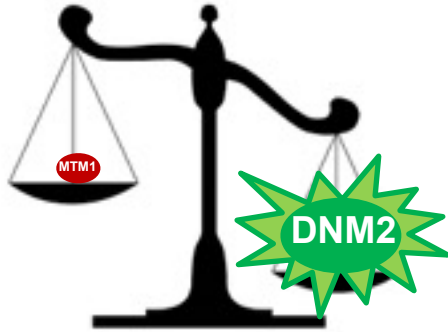
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# Cross therapy

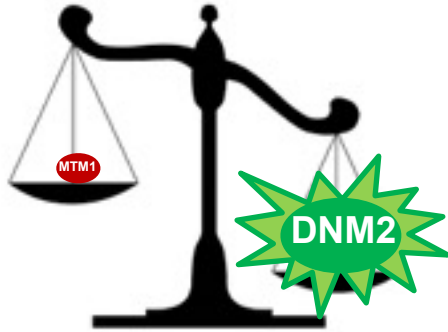
## Idea and applications



**Myotubular myopathy:  
MTM1/DNM2 imbalance in muscle**

# Cross therapy

## Idea and applications

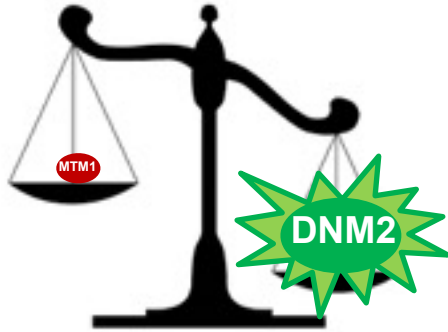


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**→ Reduction of DNM 2 as therapy?**

# Cross therapy

## Idea and applications



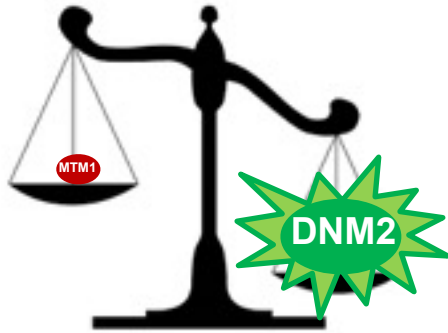
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**Mice without MTM1 and less DNM2:  
normal life span + almost normal force**

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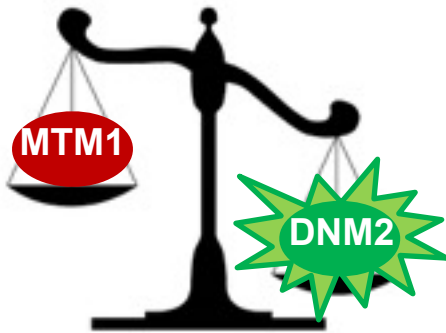
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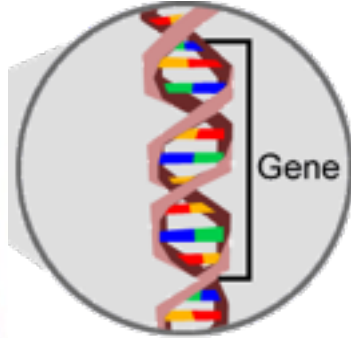
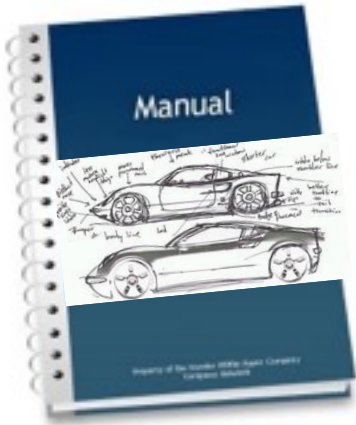


Centronuclear myopathy:  
Similar MTM1/DNM2 imbalance in muscle

Same therapeutic approach for MTM / CNM?

# How could we reduce DNM2 in patients?

In mice we removed DNM2 genetically

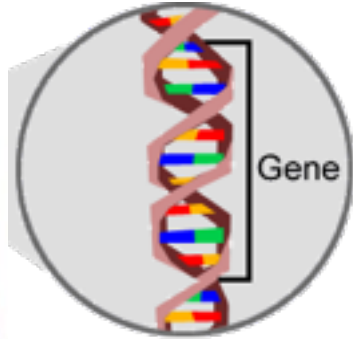


A gene is a fragment of a chromosome  
It carries the information for a protein

**DNM2 is like a manual to build a car**

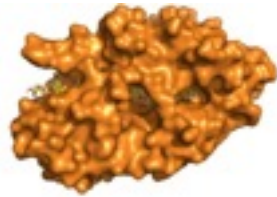
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A protein has an activity in the cell

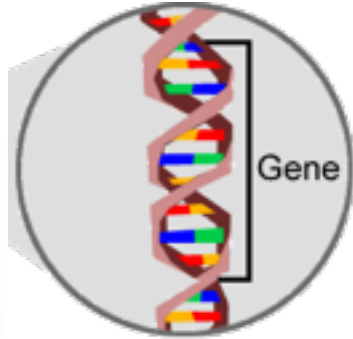
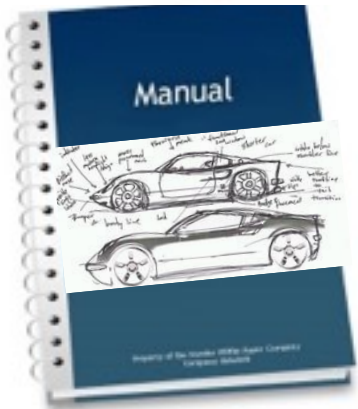
**Dynamamin 2 is the car**

**Two possibilities to reduce DNM2**

1. At the DNA level: produce less dynamin

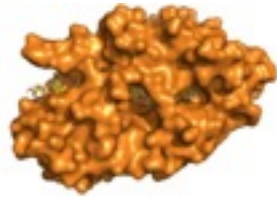
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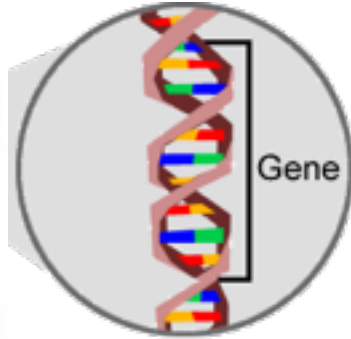
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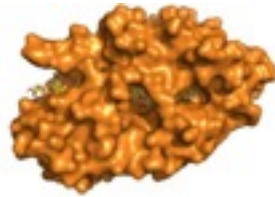
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A protein has an activity in the cell  
**Dynamin 2 is the car**

## Two possibilities to reduce DNM2

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

