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

![Diagram showing the exons and mutations of DNM2 with associated phenotypes and percentages.](image)

- **Exon 8**
  - R368K
  - Neonatal
  - Intermediate
  - 20%
  - R369W
  - Child/adult
  - Variable
  - 10%

- **Exon 11**
  - R465W
  - Childhood
  - Moderate
  - 25%

- **Exon 14**
  - R522H
  - Adult-onset
  - Mild
  - 10%

- **Exon 16**
  - S619L
  - Neonatal
  - Severe
  - 10%
Nuclei during muscle development

Nuclei during muscle development

muscle cells → fusion → myotube → maturation → muscle fiber
Nuclei during muscle development

- **fusion**
- **maturation**

- muscle cells
- myotube
- muscle fiber

section
Nuclei during muscle development

"myotubular myopathy"

muscle fibers look like myotubes before maturation
Nuclei during muscle development

muscle cells, T-Tubules (MTM1, BIN1, DNM2 involved) involved in muscle structure

myotube, T-Tubules (MTM1, BIN1, DNM2 involved)

muscle fibers

section

“myotubular myopathy”
muscle fibers look like myotubes before maturation

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

Structure determines function
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Structure determines function
Cross therapy
Idea and applications

Myotubular myopathy:
MTM1/DNM2 imbalance in muscle
Cross therapy
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Reduction of DNM 2 as therapy?
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Mice without MTM1 and less DNM2:
normal life span + almost normal force
Cross therapy
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Myotubular myopathy:
MTM1/DNM2 imbalance in muscle

Reduction of DNM 2 as therapy?

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

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
How could we reduce DNM2 in patients?

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

DNM2 is like a manual to build a car.

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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Two possibilities to reduce DNM2

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