MUSCULAR DYSTROPHIES RELATED TO DYSTROPHIN IN DOGS. MOLECULAR BASIS AND THERAPEUTIC STRATEGIES.

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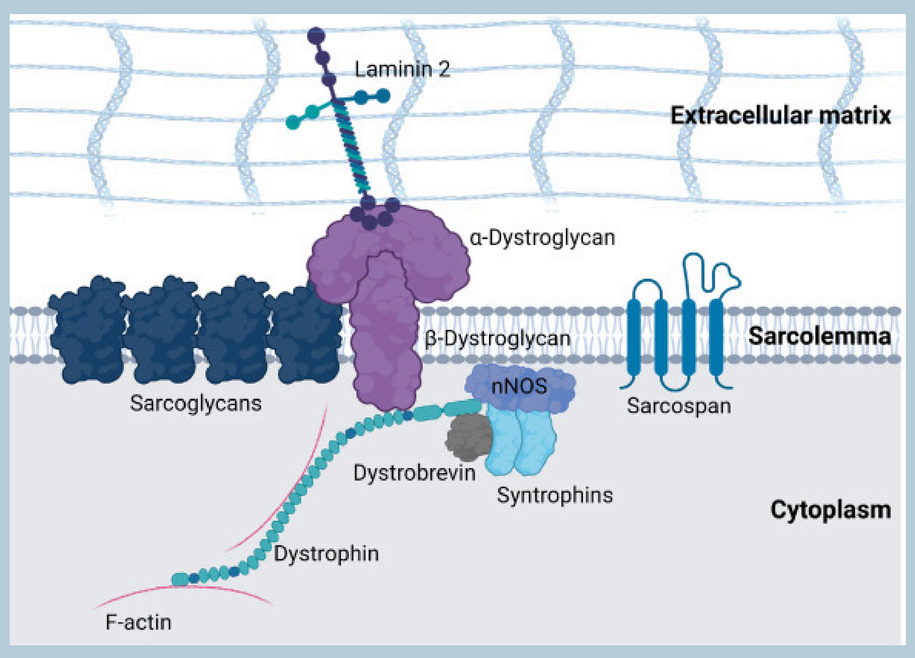
OBJECTIVE

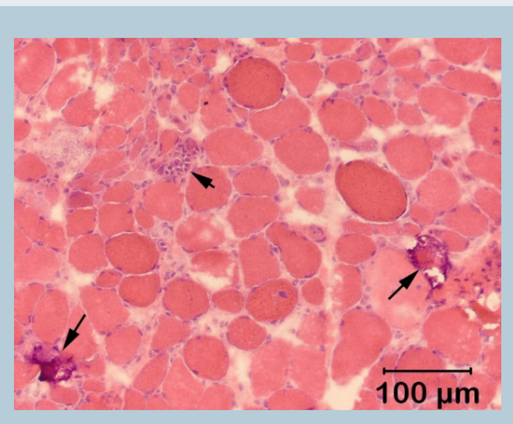
- Explain the clinical signs of dystrophin-related dystrophies in humans and dogs.
- Most common genetic alterations causing these dystrophies.
- Conventional therapy currently used and experimental therapies under study.
- Importance of large animal models as bridges in clinical trials between mice and humans.

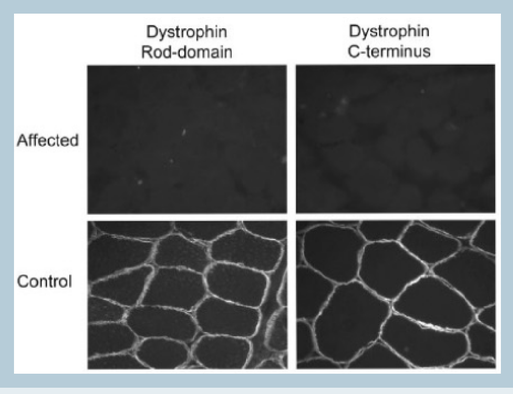
MOLECULAR BASIS



CLININAL PRESENTATION

- Human
  - Duchenne = Lack of dystrophin
    - Diagnosed < 4 years old
    - Weelchair 12 yeras old
    - **Life expectancy 30 years old**
  - Becker = Less/partially functional dystrophin
    - Severity varies
- Golden Retriever muscular dystrophy
  - Fulminant
  - Clinical sigs appear around 8 weeks
  - Clinical signs stabilize at 6 months.



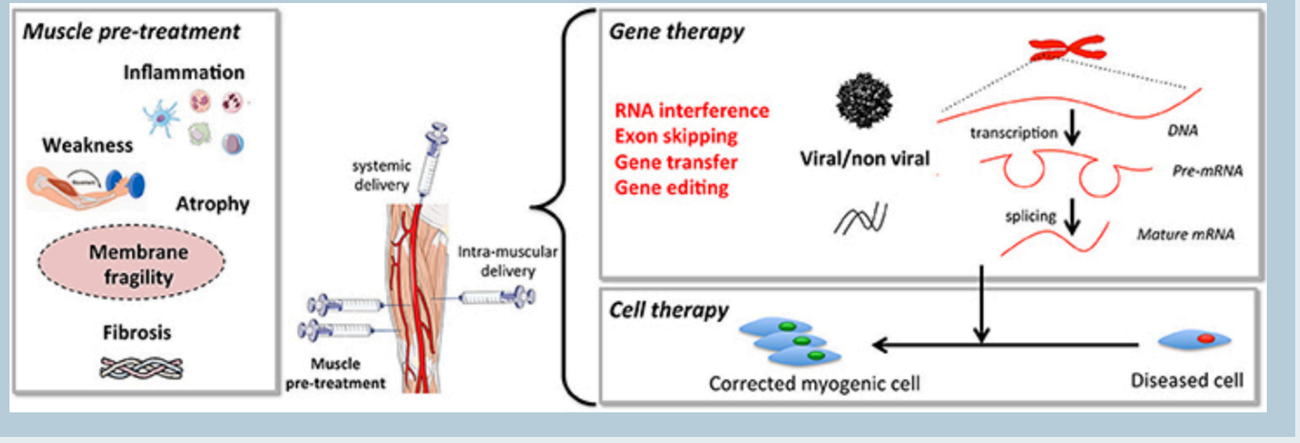


GENETIC ALTERATIONS

- **The in-frame and out-of-frame theory explains 92%** of the genetic alterations.
  - Out-of-frame = Duchenne muscular dystrophy
  - In-frame = Becker muscular dystrophy
- **70%** of mutations are **deletions or duplications.**
- 30% are point mutations.
- One-third of mutations occur *de novo*.
- Hot spots
  - Humans = 45-53
  - Dogs = 3-7 / 45-53
- The **size of the deletion is not equivalent to the severity** of the disease.
- Alternative splicing in dogs --> Stabilization of the syntoms

THERAPY

- Costicosteroids
- Personalized medicine
- In October 2023, the EMA and the FDA approved a drug called "Agamree."
- In June 2023 the FDA has approved the use of an AAV, marketed under the name "Elevidys."



CONCLUSION

Duchenne muscular dystrophy (DMD) is a severe disease with no cure. Promising therapies like **CRISPR and microdystrophins** require clinical trials to ensure safety and efficacy. While mdx mice are key in early research, **canine models better bridge** the gap to human trials. Further study of canine dystrophies can advance treatments for both humans and animals, improving quality of life across species.