

# Neuromuscular research.

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# Muscle research

- Muscle is one of the most complex systems in the body: its properties are not yet fully known.
- Several features complicate research:
  - The different kinds of muscle have unique features.
  - Muscle is “controlled” by a complicated series of genes, turning on & off, making proteins as needed.
  - Muscle displays a very complicated developmental pathway – muscle in early development differs considerably from adult muscle.
  - There is a complex balance between muscle degeneration from use, injury, disease & aging vs. regeneration and replacement with new muscle.

# Balancing growth involves many factors

- A complex balance between growth inhibitors and growth promoters is maintained.
- One major challenge is to discover the many factors that control ( $\downarrow$   $\uparrow$ ) the growth of muscle.
- This control is orchestrated by a network of signals, genes and the proteins they produce.
- Considerably more research is needed just to understand normal muscle development, control of production, and muscle function.

# Today - 1

- Many basic questions remain to be answered:
  - How does normal muscle develop and function?
  - What are the complex relationships between muscle and other systems in the body, for example, between muscle and the immune system?
  - How does normal muscle recover after injury?
  - Researchers must understand the complex network of genes that control muscle growth and health.
  - Why & how does muscle mass decrease with age so much?

# Today - 2

- Muscle disorders present a complex picture:
  - There are ~40 major types & many more subtypes.
  - Many of these disorders:
    - remain difficult to diagnose,
    - are not well understood in terms of causes or mechanisms – how is the muscle affected?
  - Very few direct treatments have been developed.
  - While many of these disorders involve genetic mutations, gene therapy is in its earliest stages and several significant setbacks have occurred.
  - Several other muscle disorders involving the immune system appear to be equally challenging.

# Medical research is incremental

- Many small steps lead to practical successes.
- Generally speaking, advances in diagnosis precede advances in treatment.
- Typical steps:
  1. Understanding normal function.
  2. Description of a disorder.
  3. Clinical (basic) diagnosis.
  4. Discover the cause/mechanism of pathology.
  5. Develop a reliable and accurate test/diagnosis.
  6. Develop a specific treatment.

# From bench to bedside

- A major discovery in the laboratory today may still take years before clinical applications.
- A system of clinical trials tests new treatments.
  1. Phase 0: tests done in the lab and on animals.
  2. Phase I: a small study to determine safety.
  3. Phase II: larger studies of safety / side effects.
  4. Phase III: large controlled studies on groups of patients to see how well it works in practice.
  5. Phase IV: watch for long-term side effects.

# Long-term

- Researchers would like to understand the cause and mechanism of each muscle disorder.
- Many of these causes will involve the understanding other body systems (the immune system, genes ↔ protein production, etc.).
- Each disorder will have a specific treatment developed to address its impact/symptoms.
- Ultimately, disorders will be identified and corrected before major damage occurs.

# Research time frames

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- Although medical research is making tremendous advances, our long-term muscle research goals remain in the distant future.
- This is not what we want to hear – the slow pace of basic muscle research is very frustrating, especially for patients and their families.

# Interim strategies - 1

- Until the ultimate answers are obtained, it is likely that two strategies will be common:
- 1). Treatments designed to increase muscle function will be developed, although the underlying disease will not be affected.
  - Muscle growth factors will be manipulated to produce more muscle to compensate for disease (but not enough to create unwanted side effects).
  - Function may not be totally restored to “normal” but should provide a much improved quality of life.
  - This approach will likely be “the next step” in treatment for most muscle disorders.

## Interim strategies - 2

- 2). Often several different research and treatment avenues are being pursued simultaneously for a disorder.
- Interim treatments will likely involve using a combination of two or more approaches to try to improve muscle function and limit the effects of the disorder.
- Similar combinations of treatments may be used for several different disorders until disorder-specific treatments can be developed.

# Research

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- Each small advance helps contribute to the ultimate solutions needed.
- The long-term costs to society of muscle related illness are tremendous, not to mention the emotional & practical costs to patients/families.
- Our support of organizations like Muscular Dystrophy Canada helps keep muscle research in the spotlight.