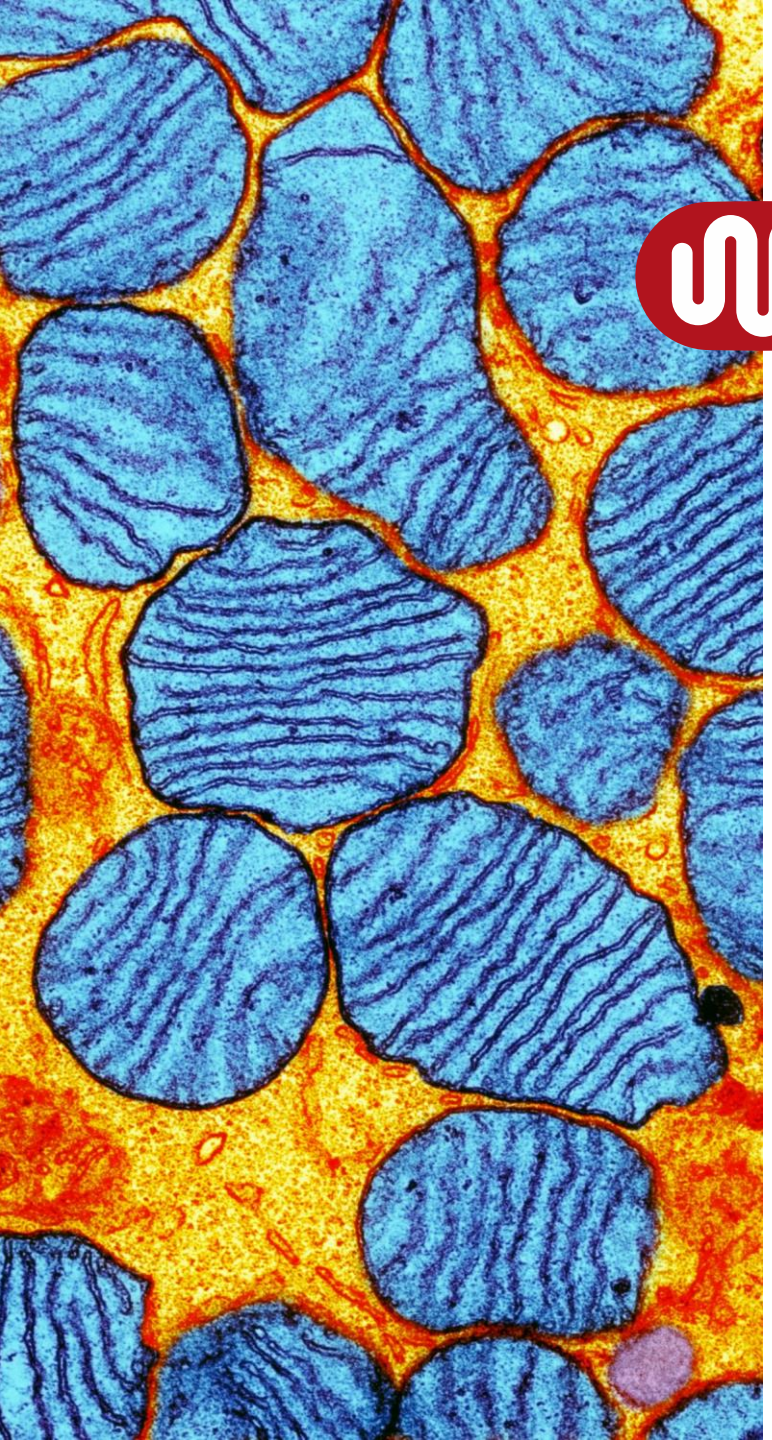

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targeting mitochondria. advancing human health.

MTB-1 MEDIATED GENE REGULATION SHOWS BENEFICIAL EFFECTS IN DMD PATIENT CELLS AND MDX MICE

PPMD 2016 Annual Connect Conference

George Mulligan, PhD
VP Translational Medicine

June 28, 2016

DISCLOSURE

I am employed by Mitobridge, Cambridge MA.

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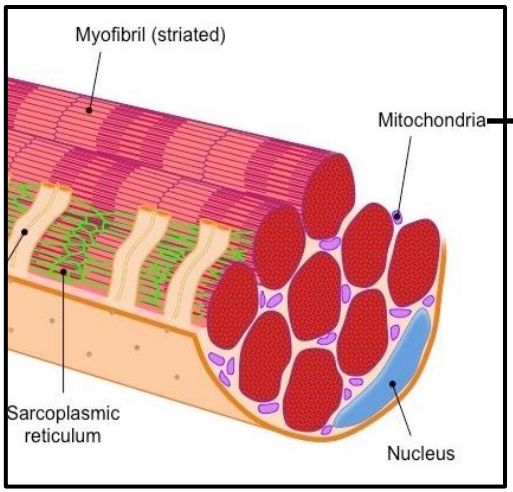
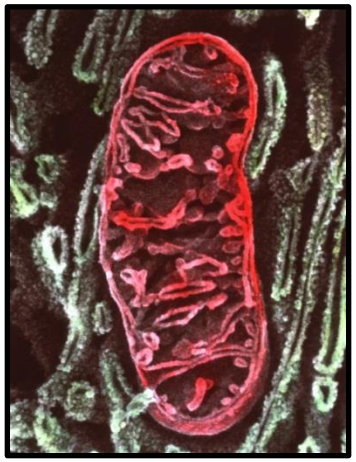
MITOBRIDGE HIGHLIGHTS

- Company launched in October 2013 with the mission to become the leader in developing therapeutics that treat a wide range of serious diseases by modulating mitochondrial function
- High-performing team of employees, advisors and consultants
  - Renowned group of founding scientists
  - Experienced management team
  - Accomplished investor syndicate
  - 29 full-time chemists, biologists and pharmacologists with drug discovery expertise
- Strategic relationship with Astellas shapes the 5 year R&D plan

MITOCHONDRIA ARE CRITICAL FOR MUSCLE HEALTH





✓Energy production

✓Cell death regulation

✓Cell communication

- Mitochondria are organelles found in most cells; play a critical role as energy source through production of ATP
- Mitochondrial dysfunction can cause or contribute to cellular pathologies that cause serious diseases

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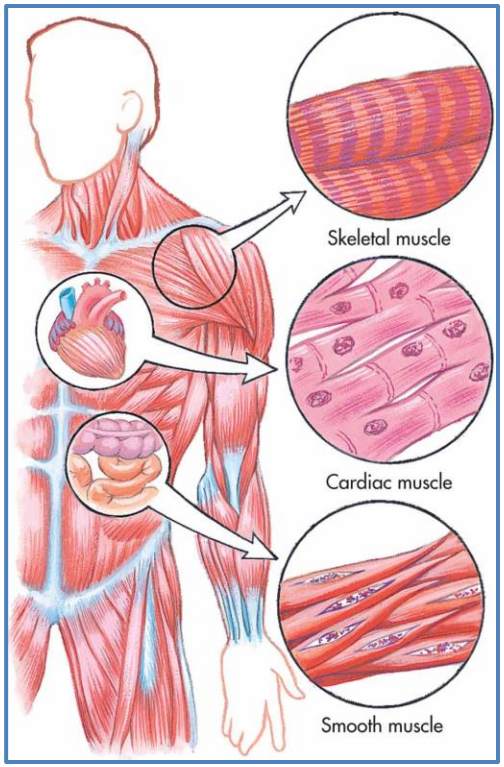
MITOCHONDRIAL DYSFUNCTION IN DMD

- Numerous studies show mitochondrial dysfunction is involved in and contributes to abnormalities in dystrophic muscle *
  - Effects of impaired mitochondrial function in muscle
    - Reduces ability to work for long periods (endurance)
    - Increases inflammation
    - Triggers cell death
  - Impaired function can be measured by reduction in ATP, reduced oxygen consumption and other parameters
- Mitochondrial impairment is also evident in cells and tissues from mdx mice, a model of DMD

*Select references
Scholte and Busch (1980)
Carroll et al. (1985)
Chen et al. (2000)
Baron et al. (2011)
Rybalka et al. (2014)
Timpani et al. (2015)

IMPROVING MITOCHONDRIAL HEALTH BENEFITS MULTIPLE TISSUES

- Certain exercise regimens can improve mitochondrial functions in muscle
  - Increase use of fatty acids to make more ATP/ energy
  - Improve blood flow
  - Produce new mitochondria - biogenesis
- Improvements in mitochondrial function can extend beyond skeletal muscle
  - Cardiovascular (energy in heart muscle)
  - Respiratory functions (energy in diaphragm)



- Mitobridge's drug candidate regulates the cellular processes induced by exercise regimens

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MTB-1: A NOVEL DRUG CANDIDATE FOR DMD

- Small-molecule compound, oral once-daily dosing
- Regulates genes that produce proteins essential for mitochondrial activities
- Studies in DMD patient muscle cells and mdx mice demonstrate the compound is active at dose levels that are well-tolerated
- Compound could provide benefit for all DMD patients regardless of dystrophin mutation type
- Novel mechanism for DMD
- Currently in late-stage preclinical development

MTB-1 EFFECTS IN CELLULAR AND ANIMAL MODELS OF DMD

- In DMD patient cells and mouse muscle cells, MTB-1
  - Increases expression of genes and protein that enhance mitochondrial function
  - Increases numbers of mitochondria in muscle cells (biogenesis)
  - Increases oxygen consumption
- In mdx mouse model of DMD, MTB-1 administration (orally) for 5-7.5 weeks
  - Improves skeletal muscle
    - Reduces level of damage
    - Reduces inflammation & dying cells
    - Increases numbers of regenerating cells
  - Improves diaphragm
    - Reduces fibrosis and numbers of dying cells
  - Increases voluntary activity and endurance
    - Increases rearing activity
    - Increases time and distance on treadmill run

TRANSLATING PRE-CLINICAL RESULTS INTO POTENTIAL DMD PATIENT BENEFITS

	DMD disease characteristics	Effect of MTB-1 in mdx model and DMD patient cells
Cellular	• Dysfunctional mitochondria • Defective muscle bioenergetics • Defective fatty acid oxidation	• Increase in mitochondrial number and oxygen consumption rate in DMD patient cells
Tissue	• Muscle degeneration • Inflammation • Muscle fibrosis	• Decrease degeneration & cell death • Decrease inflammation • Increase regenerating cells • Decrease diaphragm fibrosis
Functional	• Muscle fatigue • Muscle weakness • Exercise intolerance	• Increase rearing activity • Increase endurance

A POTENTIAL NEW THERAPEUTIC FOR DMD

- Novel mechanism: MTB-1 activates cellular pathways that improve mitochondrial function in impaired muscles
- Demonstrates significant efficacy in DMD patient cells and mdx mouse model
  - Increase in energy production
  - Increase in functional endurance
  - Decrease in diaphragm fibrosis
  - Improve muscle tissue morphology
  - Well tolerated in animal studies
- An oral agent that addresses multiple symptoms of DMD regardless of dystrophin mutation type
  - Potential for combination with other treatments
- Developing clinical plan in partnership with Astellas Pharma