

**Myotonic Dystrophy Foundation Annual Conference
San Francisco
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“Myotonic Dystrophy and Sleep”

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Disclosures

In addition to funding from NIH/NINDS, MDA, SMAFoundation, MDFoundation, in the past 12 months I have had the following financial relationships with the manufacturers of commercial products or providers of commercial services possibly discussed in this presentation:

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- Athena Diagnostics – royalties for licensed technology
 - Audentes, Inc. – consultation
- Santhera Pharmaceuticals – consultation

Athena Diagnostics Royalties for DM2 and SCA5 genetic testing

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DM Research at Stanford

- Sleep and CNS evaluations in young myotonic dystrophy adults
- Coordinated clinical and animal studies of CNS in DM with University of Florida (Swanson, Ranum) and Stanford Sleep Center (Mignot, Nishino)
- Specimen Repository
- Investigation of DM changes in neuropsychology, MRI, Electrophysiology, CSF, blood biomarkers

Conclusions

- **Myotonic Dystrophy (DM) affects many body systems that directly or indirectly alter sleep**
 - **Altered throat and breathing musculature can reduce sleep quality**
 - **Direct effects on brain sleep centers can alter sleep patterns and quality of sleep**
- **Abnormal sleep in DM affects behavior, cognition and quality of life**
- **Treatments may improve sleep quality in DM**
- **Research is shedding light on DM sleep including CNS causes and effects**

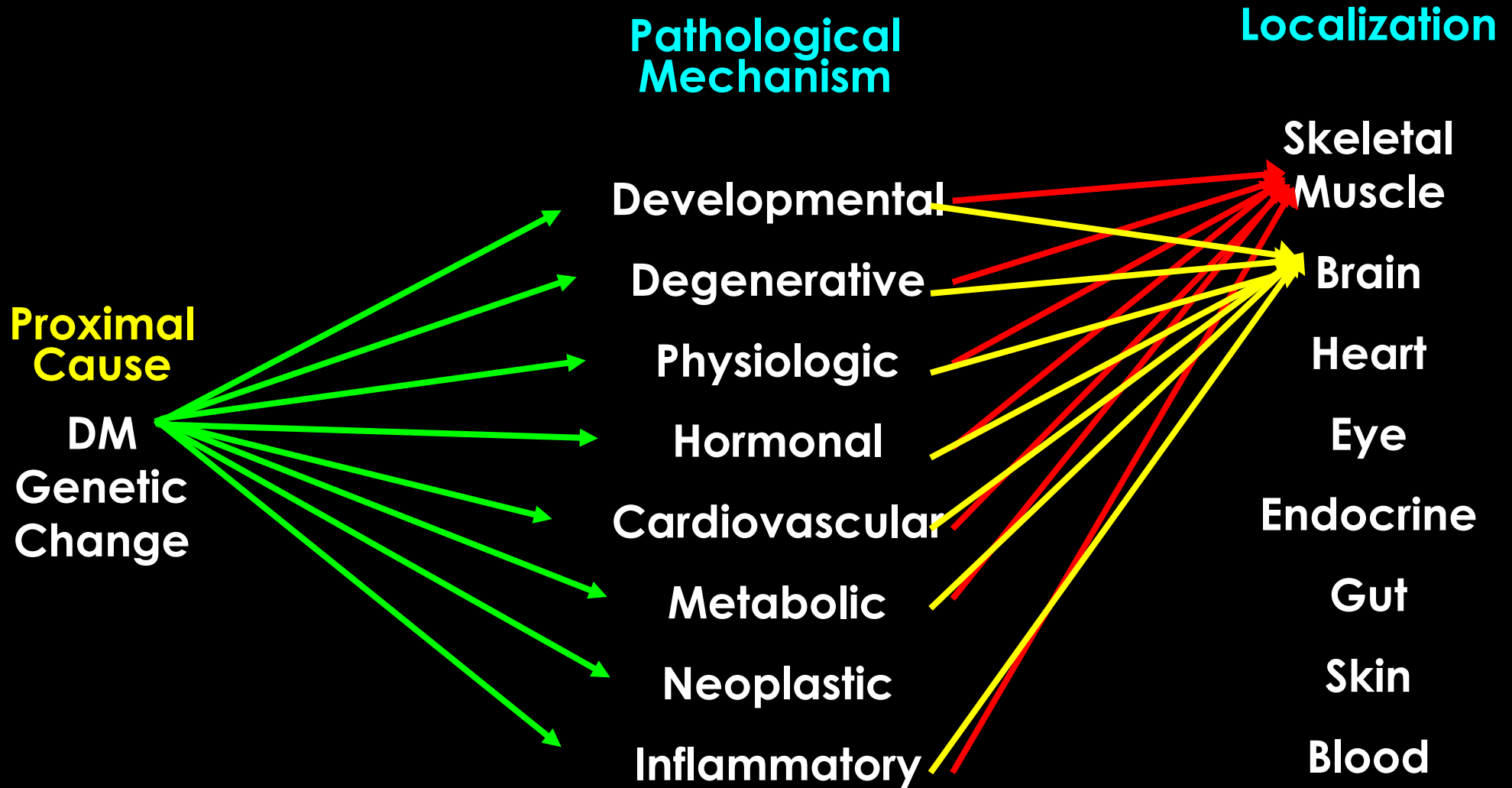
Organization of Talk

- Global effects of DM and how they impact sleep
- Specifics of sleep abnormalities in DM
- Ongoing DM Sleep Research
- Questions (and Answers?)

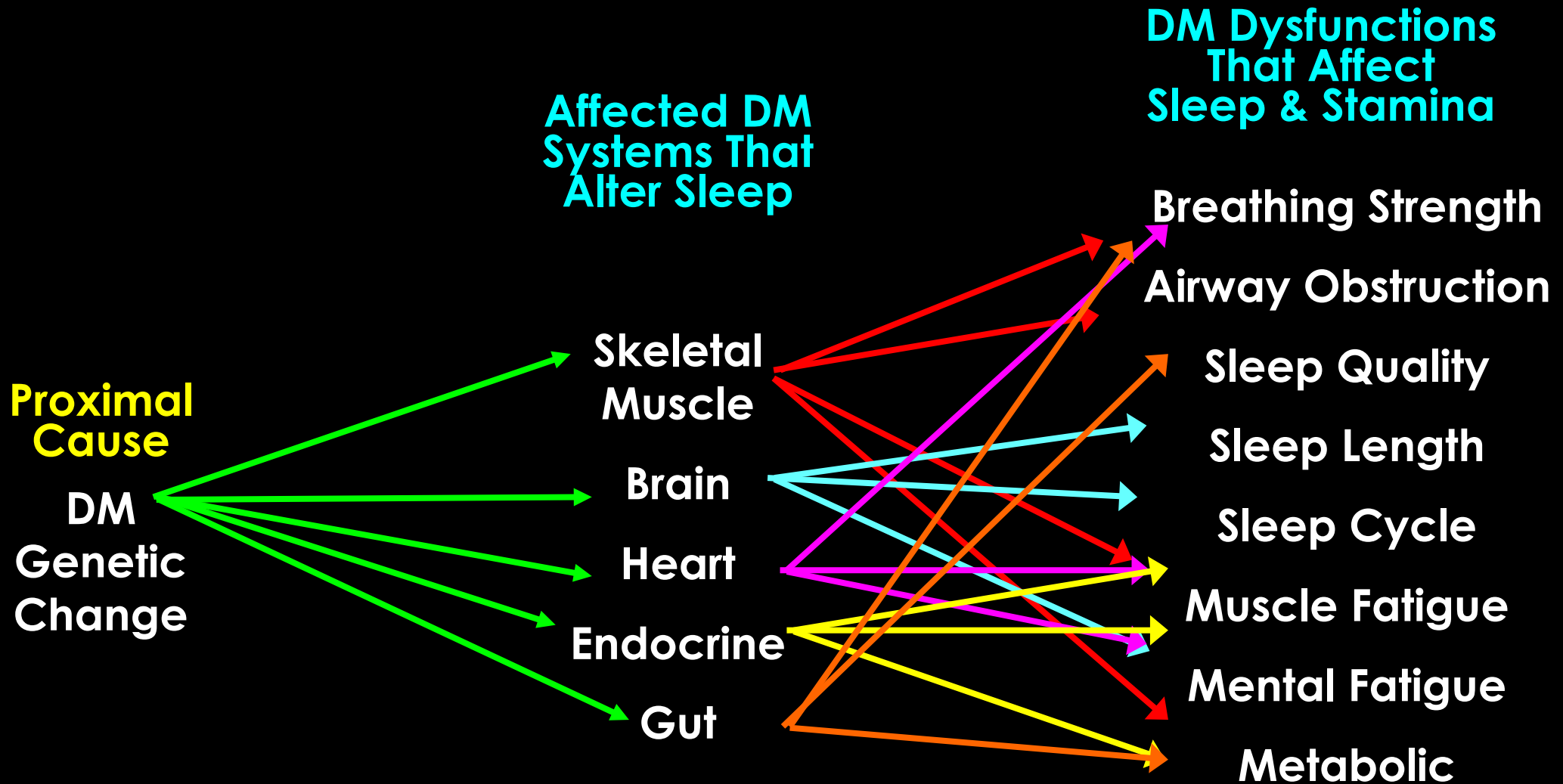
First – Questions for the audience

- **For individuals with DM (directly or family report)**
 - **How many, at some time, have been told to use breathing support at night (e.g., CPAP, BiPAP, AVAPS, Curiass)**
 - **How many actually ever tried it?**
 - **How many continue(d) to use it?**
- **How many have been prescribed a stimulant to combat daytime sleepiness (Provigil/Nuvigil/modafinil; Ritalin/dexedrine; Cylert/pemoline)?**
 - **How many have ever tried it?**
 - **How many continue to use it?**

DM Clinical Features

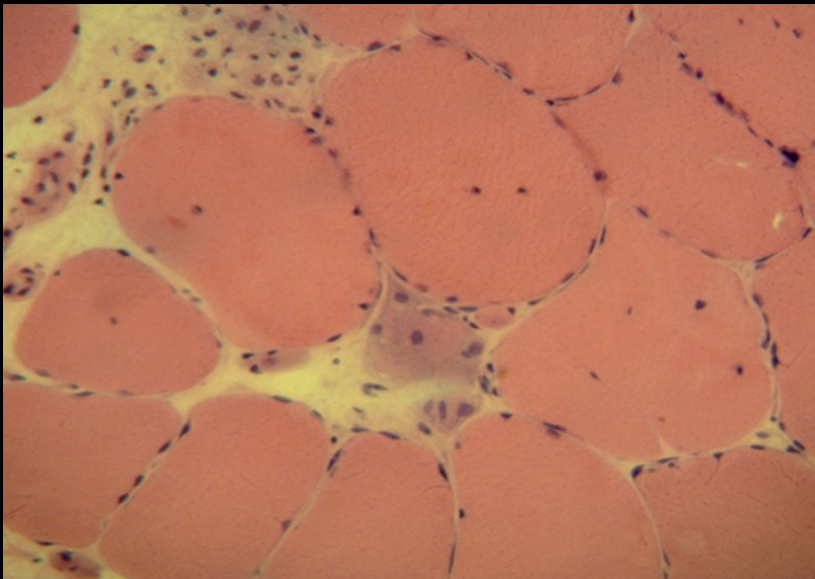
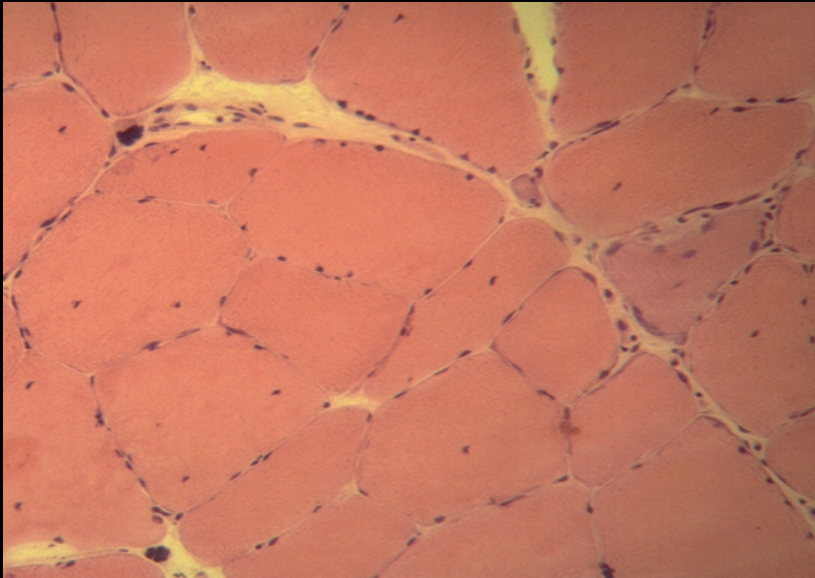


DM Alteration of Sleep



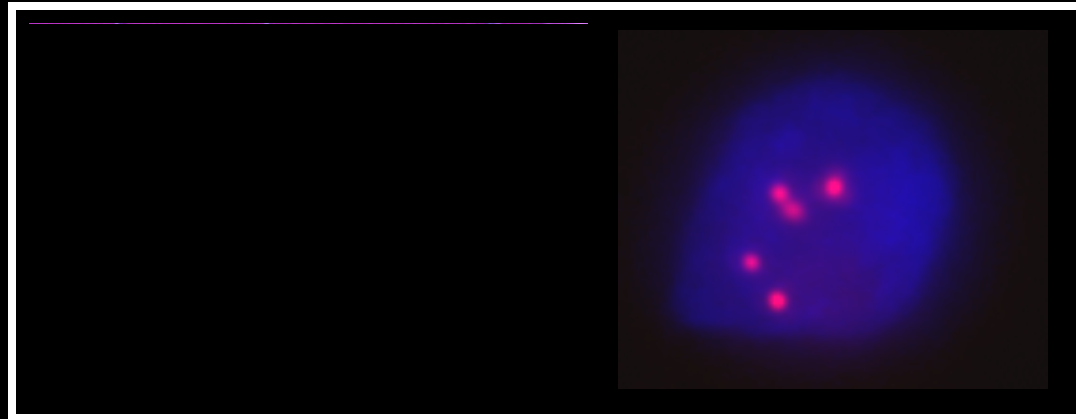
DM muscle pathology

- muscular dystrophy**
- congenital myopathy**
- metabolic myopathy**
- myotonia**

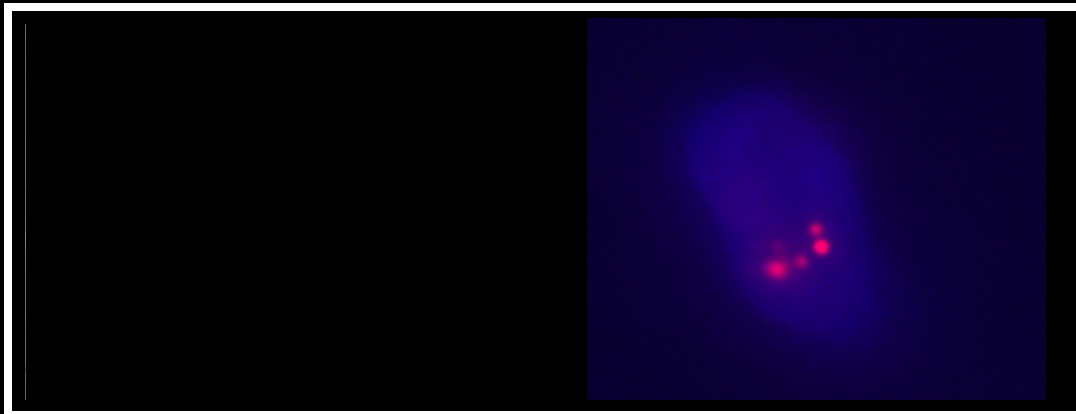


RNA Changes Precede Pathology

**Muscle
Bx @
28y/o**



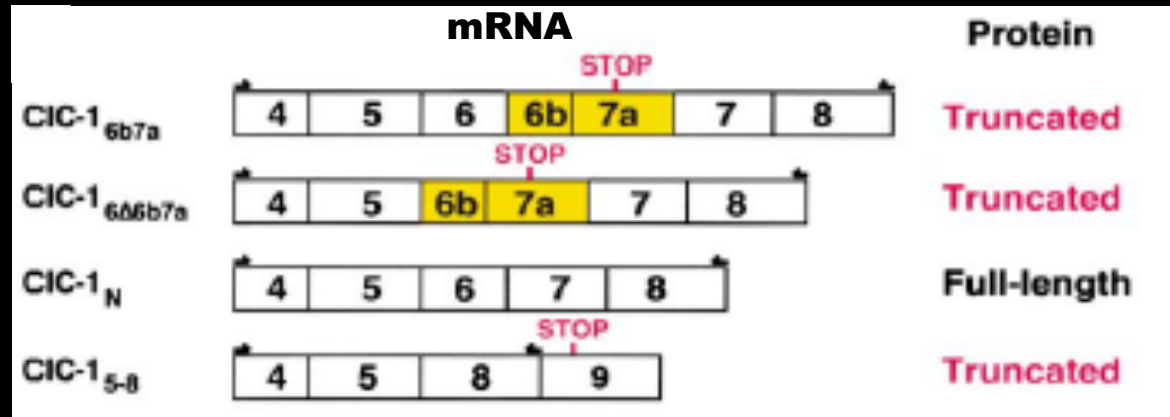
**Muscle
Bx @
36y/o**



Savkur, et. al. AJHG, 74:1309; 2004

How is CIC-1 altered in DM?

Alternate Splicing



Charlet-B, et. al., Mol Cell, 10:45, 2002

CIC-1 Immunofluorescence

Mankodi, et. al., Mol Cell, 10:35; 2002



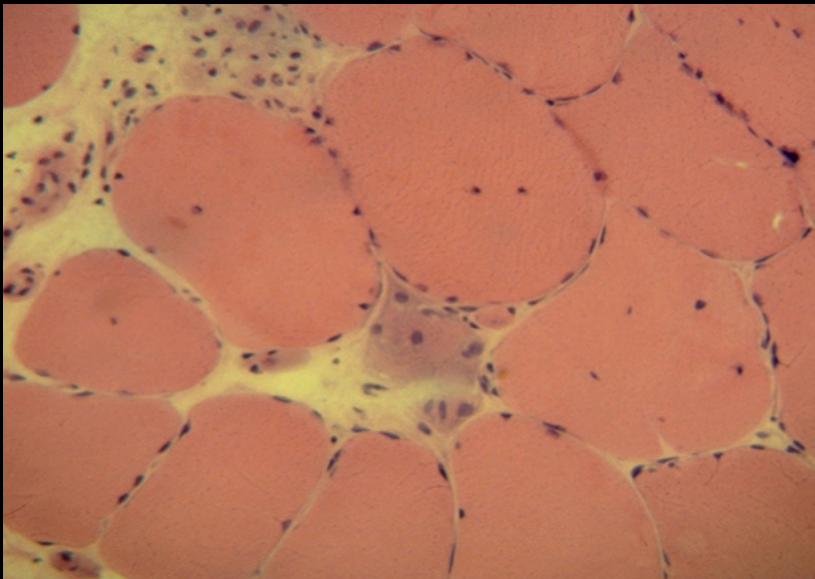
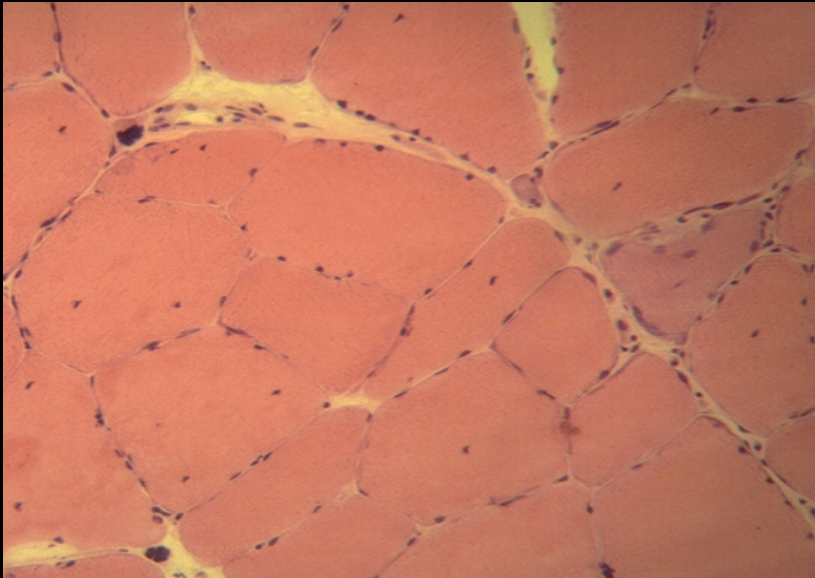
Normal

DM1

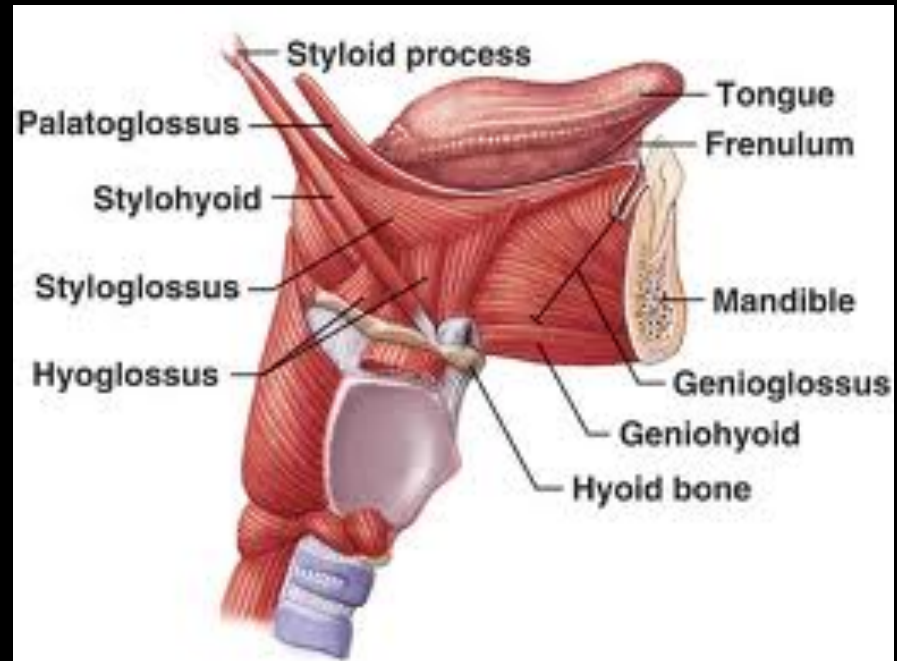
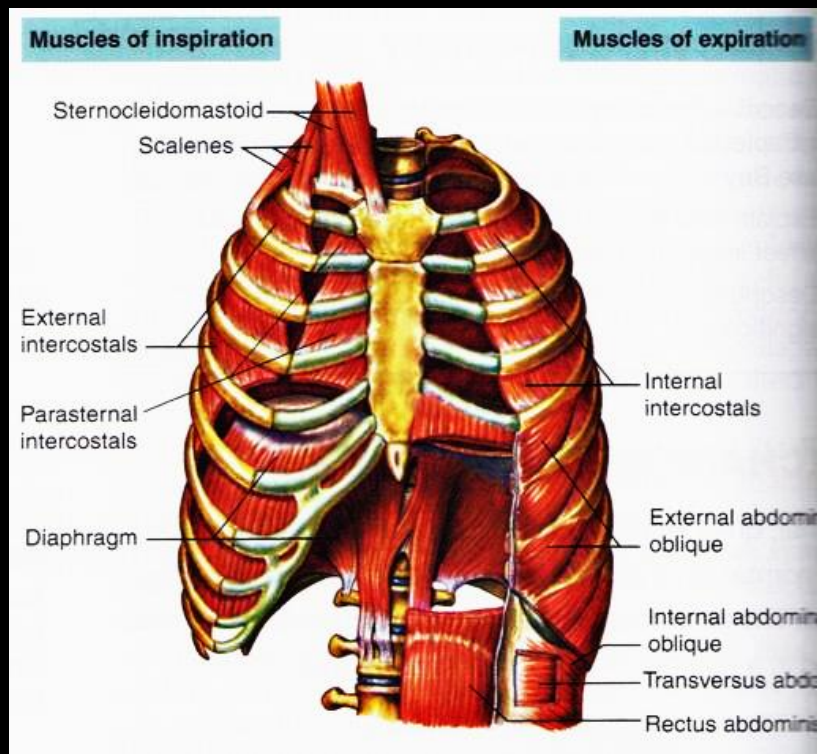
DM2

DM muscle pathology

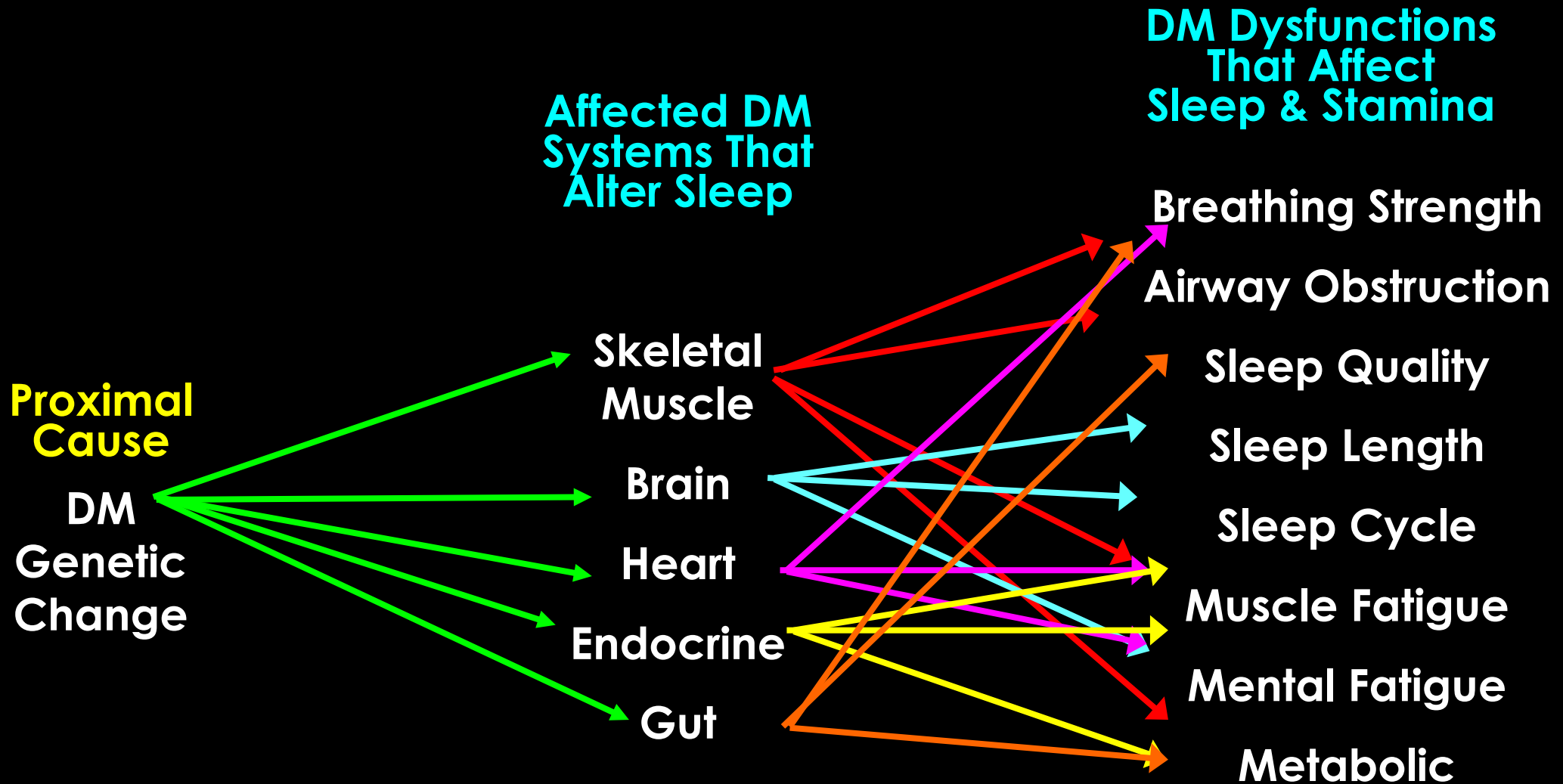
- congenital myopathy**
- muscular dystrophy**
- metabolic myopathy**
- myotonia**



DM Muscle Involvement Directly Affecting Sleep



DM Alteration of Sleep



What do DM patients experience regarding sleep?

- Greater than normal need for sleep
- Inability to awaken quickly
- Snoring, dry eyes, dry mouth during sleep
- Fragmented sleep patterns
- Excess or abnormal sleep movements
- Sleep paralysis or sleep-related hallucinations or excessively vivid dreams
- Self-medication or prescriptions to wake-up or fall asleep

Conclusions

- **Myotonic Dystrophy (DM) affects many body systems that directly or indirectly alter sleep**
 - **Altered throat and breathing musculature can reduce sleep quality**
 - **Direct effects on brain sleep centers can alter sleep patterns and quality of sleep**
- **Abnormal sleep in DM affects behavior, cognition, quality of life, and overall health (heart, energy, etc.)**
- **To treat sleep abnormalities in DM**
 - **Provide excellent comprehensive baseline care**
 - **Thoroughly evaluate and determine cause of sleep disorder**