Integrating basic research with genomic discoveries to provide clinical and pre-clinical insights.

New Mouse Models of Myotonic Dystrophy

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Most slides courtesy of:  
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JAX Labs
Mice with Neurological Disorders Have More Treatment Options than Ever Before

Does every disease known to mouse-kind have a “treatment?”

Change the dynamic; better mice & using them better
So, Why New DM Mice?

• Need for better model for studies of disease mechanisms & for preclinical drug testing
• Genetic stability ($\text{HSA}_{LR}$ mouse shows reduction in repeat length over time)
• Better symptom profile (including brain)—$\text{HSA}_{LR}$ only has the repeat in muscle & muscle wasting is modest
• Access—available when needed, in whatever numbers, without licensing charges
Working with Jackson Laboratory (JAX)

To discover precise genomic solutions for disease and empower the global biomedical community in our shared quest to improve human health

**JAX researchers**
- 1,700 employees over 3 campuses
- 287 Ph.D.s, M.D.s, and D.V.M.s, including:
  - 50 Professors, Associate Professors and Assistant Professors
  - 55 Research Scientists and Research Associates

**Mouse Resources**
- About 2.8 million JAX Mice distributed annually
- JAX® Mice have been shipped to approximately 20,000 investigators in more than 900 institutions, in 56 countries
- More than 7,000 varieties are available as breeding mice or frozen embryos.
Repeat Expansion Diseases

• Creating mouse models for repeat expansion diseases can be challenging

• Repeats tend to contract when cloned into *E. coli*

• Knock-In of repeats into the mouse locus are informative

• Mice carrying Human BACs with expansion repeats are important tools in preclinical research
Creating BAC Transgenic Models of DM1

- Start with DNA from patients with high expanded repeats isolated from fibroblasts
- Create a BAC library and screen for BACs carrying full length genes and high repeat expansions
- Grow small cultures and select for preps with high repeats
- Grow larger cultures for DNA prep
- Perform pronuclear injection
- Screen numerous founders for full length genes and high repeats
- Select for germ line transmission
- Characterize new mouse models
- Immediately make available to the scientific community
Using the Mice Better

• Rigorous design of preclinical drug testing
• Careful interpretation of data
• DM field needs to work to improve how preclinical testing is done