

# New Mouse Models of Myotonic Dystrophy



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**Most slides courtesy of:  
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Integrating basic research with genomic discoveries to provide clinical and pre-clinical insights.

# 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



[skateboardpets.com](http://skateboardpets.com)  
<http://go.tunpic.hu>





# So, Why New DM Mice?

- Need for better model for studies of disease mechanisms & for preclinical drug testing
- Genetic stability (HSA<sub>LR</sub> mouse shows reduction in repeat length over time)
- Better symptom profile (including brain)—HSA<sub>LR</sub> 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.



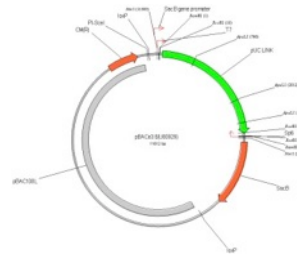
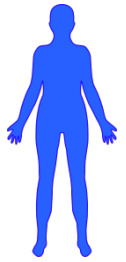
# Repeat Expansion Diseases

- 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

