

## Spring 2011 Exam 1 Abstract

*This abstract will be part of the first exam. You do not need to read the actual paper. Your goal before the exam is to make sure you understand the concepts and ideas presented in the abstracts. You may talk with friends (in fact I hope that you do) and ask me anything about the information presented below.*

Gomes-Preira *et al.* (2007) CTG trinucleotide repeat "big jumps": large expansions, small mice. *PLoS Genetics* 3(4):e52.

Trinucleotide repeat expansions are the genetic cause of numerous human diseases, including fragile X mental retardation, Huntington disease, and myotonic dystrophy type 1. Disease severity and age of onset are critically linked to expansion size. Previous mouse models of repeat instability have not recreated large intergenerational expansions ("big jumps"), observed when the repeat is transmitted from one generation to the next, and have never attained the very large tract lengths possible in humans. Here, we describe dramatic intergenerational CTG\*CAG repeat expansions of several hundred repeats in a transgenic mouse model of myotonic dystrophy type 1, resulting in increasingly severe phenotypic and molecular abnormalities. Homozygous mice carrying over 700 trinucleotide repeats on both alleles display severely reduced body size and splicing abnormalities, notably in the central nervous system. Our findings demonstrate that large intergenerational trinucleotide repeat expansions can be recreated in mice, and endorse the use of transgenic mouse models to refine our understanding of triplet repeat expansion and the resulting pathogenesis.