

Mutagenesis and Broad-based Phenotype Screening by The Tennessee Mouse Genome Consortium.

Dabney Johnson and members of the TMGC

The Tennessee Mouse Genome Consortium (TMGC) is a formal collaboration among seven institutions across the state of Tennessee to employ their academic and clinical expertise for the detection of newly induced recessive mutant phenotypes in mice.

The ORNL strategy of large-scale, phenotype-driven regional mutagenesis, primarily by the use of ENU, leads to the recovery of phenotypically significant mutations that map to specific chromosomal regions. This strategy is designed to generate from each pedigree multiple visibly-marked test class mice all carrying the identical mutagenized chromosome, permitting distribution for multi-site screening, shelving for aging/rescreening for later-onset phenotypes, and a statistically useful sample size from each pedigree tested for innately variable phenotypes.

Pilot programs have supported primary screening of nearly 700 pedigrees from experiments performed at ORNL targeting the pink-eyed dilution region of mouse chromosome 7 for visible and lethal phenotypes as well as more subtle, behavioral, biochemical, and morphological abnormalities. For primary screens for which variable scores are expected (e.g., behavior tests), four test-class mice per pedigree are scored, and pedigrees from which all four mice fall below the tenth percentile or above the ninetieth percentile relative to the entire population tested are flagged as "variant". We have confirmed as heritable five embryonic or juvenile lethals, six subtle behavioral abnormalities, and have additional potential variants in various stages of heritability testing.

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The TMGC is committed to the immediate sharing of all confirmed mutant stocks, and will supply those mice by rederivation in specific-pathogen free (SPF) conditions.