

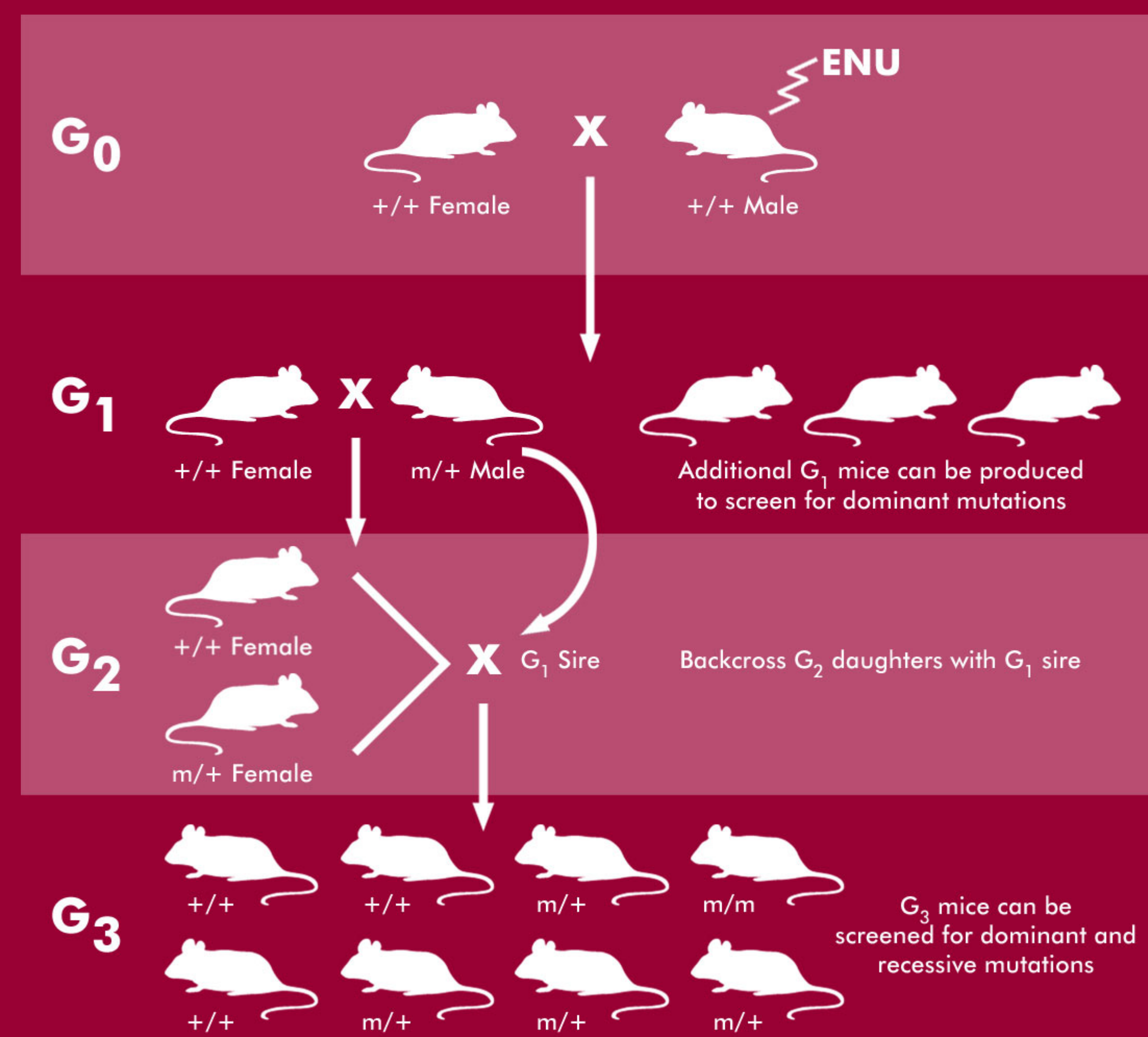
# NIH Neurogenomics Project



**Center for Functional Genomics**  
 2205 Tech Drive  
 Evanston, IL 60208  
 Contact: Jeana Yates  
 847-467-4868  
 cjs@northwestern.edu

## 1 Mutagenesis and Breeding Scheme

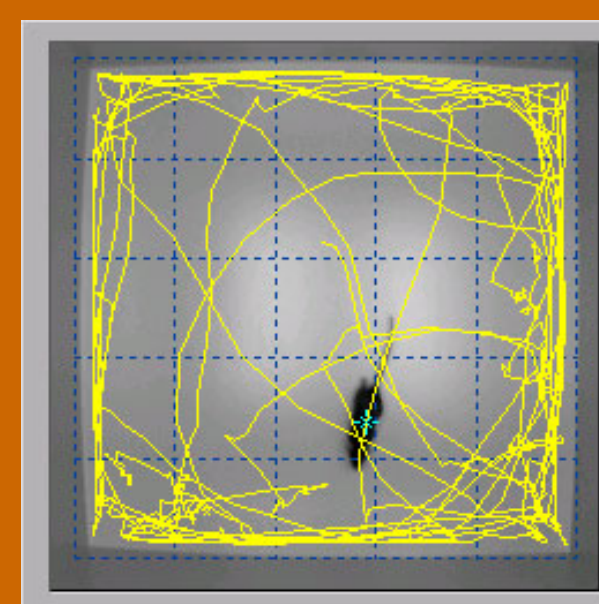
Genome-wide mutagenesis is accomplished with the chemical N-Ethyl-N-Nitrosourea. A three-generation breeding scheme is used to produce mice homozygous for induced mutations. These third generation (G3) mice are phenotypically tested so that recessive, semi-dominant, and dominant mutations can be identified.



To date, >13,000 mice have been produced and phenotypically screened. Production and screening are continuing.

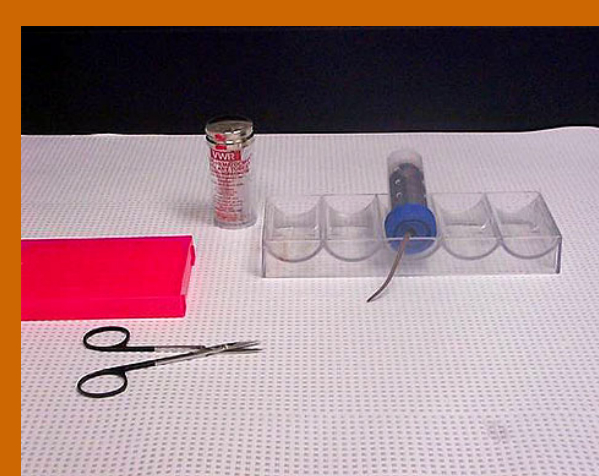
## 2 Phenotypic Testing

Mice are tested in a series of phenotypic screens focused on 5 domains. An additional set of supplemental assays comprise a "preliminary assessment." Testing is completed in ~7 weeks.



### Preliminary Assessment

The Preliminary Assessment consists of recording the animal's body weight at two ages, a hearing screen, and two emotional behavior assays: the elevated plus maze and the open field behavior.



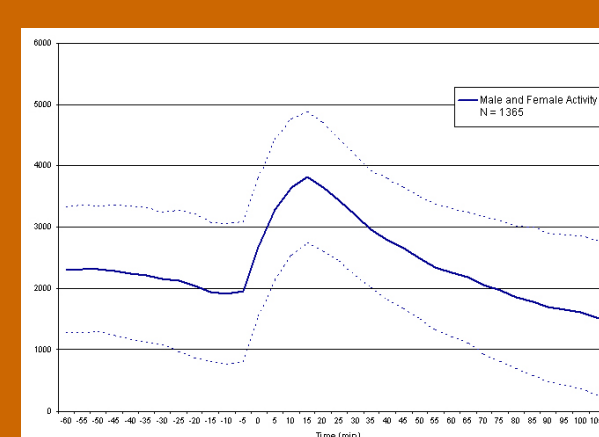
### Neuroendocrine/Stress

Serum samples are collected at the beginning and end of a standardized, acute stress (10 min restraint). Corticosterone and Thyroid Stimulating Hormone (TSH) levels are measured to assess the responsiveness of the hypothalamic-pituitary-thyroid and hypothalamic-pituitary-adrenal axes to stress.



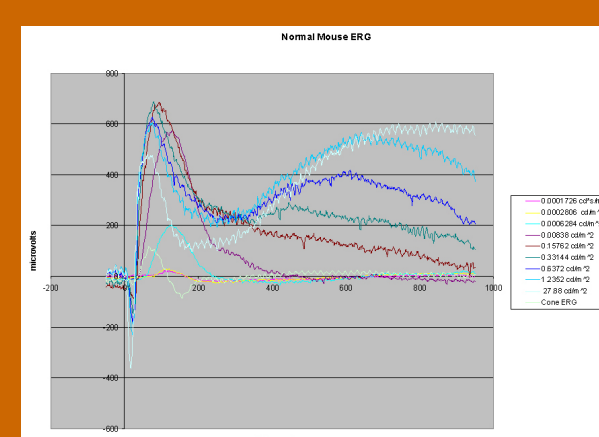
### Learning/Memory

Fear conditioning is used as a screen for learning and memory. Mice are trained to fear the test chamber with a series of four 0.75 mA footshocks, one minute apart. Twenty-four hours after training, the mice are returned to the same test chamber for 5 min and fearful behavior (freezing) is recorded as a measure of context-dependent learning or memory.



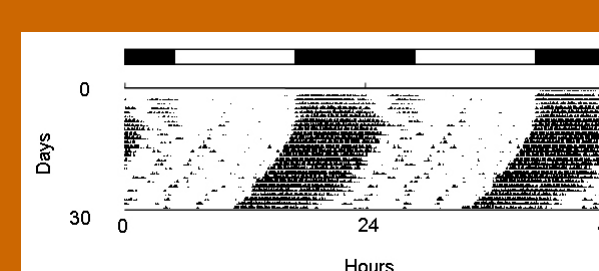
### Psychostimulant Response

The hyperlocomotion response to administration of 20 mg/kg cocaine is recorded. Drug-naïve C57BL/6J mice exhibit a robust induction of activity in response to this dose; hyper- or hypo-responsive mice are selected.



### Vision

Two assays of the visual system are used. The fundus of the eye is examined and photographed. Photos are reviewed by the ophthalmology department at the University of Iowa. Electroretinograms (left) are recorded.



### Circadian Rhythmicity

The circadian rhythm of wheel-running is monitored. Animals are maintained first in a light-dark cycle, then constant darkness (to remove time cues). The period and persistence of a free-running rhythm and phase angle of entrainment are studied.

## 3 New Mouse Lines

Listed below are examples of mutants that have been identified to date. More mouse lines can be found at [www.neuromice.org](http://www.neuromice.org).

Name	Mode of Inheritance	Description	Status
Noerg1	Autosomal dominant	All electroretinogram (ERG) responses to light are reduced or absent. Grainy fundus appearance.	Available live
part-time	Autosomal recessive	Homozygotes display ~1.8 hr shorter free-running period than wild-type.	Available live
Overtime	Autosomal semi-dominant	Heterozygotes display ~0.6 hr longer circadian period; homozygotes ~ 2 hr longer period.	Available live
tiresias	Autosomal recessive	Anophthalmic.	Under development
FCR015	Autosomal recessive	Diluted coat color, progressive ataxia, and death by ~20 days postnatal.	Under development

## 4 Investigators

Principal Investigator	Joseph S. Takahashi	Northwestern University
Mutagenesis and Production	Sandra M. Siepka	Northwestern University
Primary Screens	Martha Hotz Vitaterna Kazuhiro Shimomura Hee-Kyung Hong	Northwestern University
Neuroendocrine Responses to Stress	Eva Redei Jon E. Levine	Northwestern University
Learning and Memory	Eric Kandel Eleanor SImpson	Columbia University
Psychostimulant Response	Marc G. Caron Amy Mohn	Duke University
Vision	Lawrence H. Pinto Val Sheffield Robert Mullins Edwin Stone Edward Heffron	Northwestern University University of Iowa
Circadian Rhythmicity	Joseph S. Takahashi Fred W. Turek Sandra M. Siepka	Northwestern University
Genetics and Mapping	Kazuhiro Shimomura Martha Hotz Vitaterna	Northwestern University