

Mouse Resources Core

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A. SPECIFIC AIMS

This is a new core to INIAstress that arises out of the generation of many new mouse models through INIA support over the last 4+ years. These mouse models will be important resources to INIA investigators to study the interplay between stress, anxiety and alcohol consumption. With these new resources, we feel it is critical to disseminate them to users and evaluate each of these new mouse models with a set of INIA relevant behavioral analyses to better identify their usefulness to the various researchers in INIAstress and to the alcohol research community and beyond. The final part of this Core will provide key elements to a mouse core: distribution, cryopreservation, genotyping, and a curatorial function to keep an inventory of mouse mutants and inbred lines that we have available to INIA users and to accumulate and annotate the behavioral, cellular, and molecular knowledge about each mutant and inbred line.

The specific aims of this Core are as follows:

Aim 1 – The maintenance and distribution of novel mutant lines of mice produced by the ENU-mutagenesis program. The production and availability of novel mouse mutants that have abnormal alcohol, stress, and/or anxiety phenotypes represent an exciting resource for multi-disciplinary studies by our INIAstress investigators. This part of the Core will make these lines of mice available to INIA and community-wide researchers.

Aim 2 – The maintenance and distribution of the expanded BXD recombinant inbred (RI) and B6.A consomic lines of mice. This INIA has greatly expanded the phenotypic “space” (molecular, cellular, and behavioral) associated with unique mouse reference populations and this aspect of the Core will make these mice readily available to INIA researchers. This includes the 50 newly developed BXD RI lines that arose, in part, from the previous INIA support, and the importation of B6.A consomic lines.

Aim 3 – The Behavioral Phenotyping component of this Core will provide more comprehensive phenotypic information about EtOH and stress related behaviors in unique genetic mouse models that have been identified by high throughput behavioral screening within the INIAstress Consortium as exhibiting “extreme” phenotypes for EtOH and/or stress/anxiety responsiveness. As the behavioral screening procedures typically involve acute EtOH challenge, studies conducted in the Behavioral Phenotyping component will focus on examining neuroendocrine and behavioral consequences of stress associated with chronic EtOH exposure and withdrawal experience. In this way, data generated from this Core will serve to complement information gained from high throughput screening of these unique genetic mouse models. The genetic mouse models to be studied include: (i) ENU-induced mutants; (ii) inducible knockouts (NR2B, CRF₁, 5HT_{1A}, and CB1r); (iii) and BxD RI and B6.A strains. Specifically, the objectives of this Core are to examine the influence of stress associated with chronic EtOH exposure and withdrawal experience on:

- EtOH self-administration behavior in a model of dependence and relapse
- withdrawal-related anxiety, as measured in a battery of tests
- withdrawal-related CNS hyperexcitability, as measured by handling-induced convulsions (HIC)

-- stress responsiveness, as measured by plasma corticosterone levels

Aim 4 – Affiliated functions. There are four associated functions that are important to the operation of the MRC and INIAstress. First, is the co-ordination of distribution of mouse models to INIAstress investigators and researchers in the community. Second, in order to protect, maintain, and efficiently distribute these mouse resources for the research community, it is important to cryopreserve mouse lines as embryos. Third, it is critical to maintain quality control amongst the individual mice and mouse lines used by our researchers, and to support this function the Core will provide microsatellite and single nucleotide polymorphism (SNP) genotyping services. Fourth, in order to realize the full utilization of the resources of this Core, we will curate and disseminate information on INIA- and community-wide mouse models that are available to researchers and engage in an educational and database resource in conjunction with the Informatics Core.