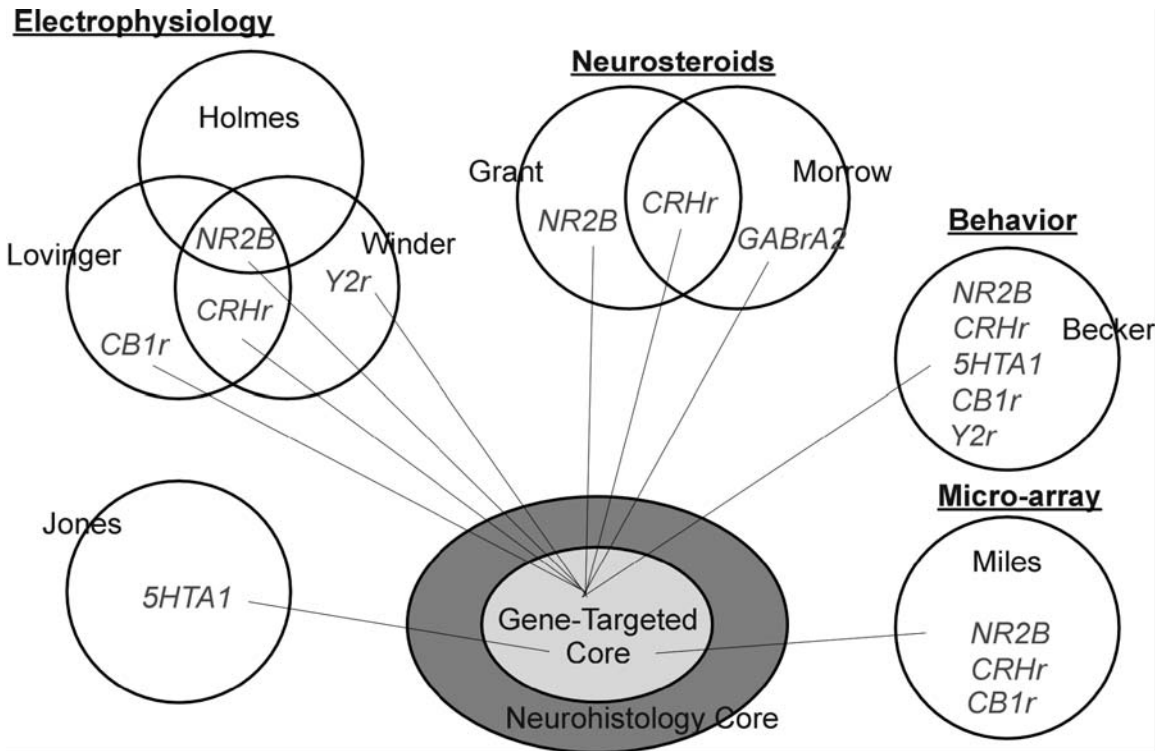


**Knock-Out Core - Gene-Targeted Mouse Core**  
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**A. SPECIFIC AIMS**

Research on the interaction between stress/anxiety and excessive alcohol consumption is a vast area of investigation. The INIAstress consortium is focusing on three general stress paradigms and two alcohol administration paradigms to characterize the role of stress/anxiety in alcohol drinking. The stress paradigms fall within three general domains: socially derived stress (isolation stress and dominance hierarchy), stress/trauma history (childhood and adult), and stress associated with chronic ethanol exposure/withdrawal (self-administration and inhalation). Stress responsiveness is evaluated on the basis of endocrinological and behavioral indices following environmental and endocrine challenges. Studies of functional changes in neurocircuits that subserve stress/anxiety and alcohol interactions interface and synergize with endocrine and behavioral measures to provide a more complete analysis of this complex relationship. Finally, the relationship of genetic factors (genotypes and functional genomics) to alcohol and stress-related phenotypes is explored through these paradigms to develop a more comprehensive understanding of the interplay between biological and environmental factors that define stress-alcohol interactions. A unique aspect of this Consortium is the translational nature of the projects, which span use of rodents, monkeys, and humans in studying the role of stress/anxiety in alcohol drinking at various levels of analyses.

The goal of the Gene-Targeted Mouse Core is to create new lines of mice for INIAstress investigators (Figure 1). This involves the creation and distribution of novel inducible knockout lines and the rapid generation and distribution of straight knockout mice using available targeted embryonic stem (ES) cell lines.



The specific Aims and objectives of this application are:

**Specific Aim 1.** *Creation* of novel inducible knockout lines. The Gene-Targeted core plans to create 5 new inducible knockout lines. We will initiate the generation of three “*floxed*” mouse line (CB1r, PY2r, GABra2) at the start of the funding period and will add two additional lines (per steering committee request) the second year.

**Specific Aim 2.** *Creation* of knockout lines from existing targeted ES cells. The short time frame (as compared to the inducible knockouts) that is needed to create straight knockouts from available targeted ES cell lines will allow us to quickly produce multiple lines of interest to INIA Investigators.

**Specific Aim 3.** *Maintain* transgenic and knockout lines and *Distribute* breeding pairs & genotyping protocols to INIA investigators.