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Abstract

[Back to Hit List](#)**Grant Number:** 5R01AA010035-04**PI Name:** HEBERLEIN, ULRIKE A.**PI Email:** ulrike@itsa.ucsf.edu**PI Title:****Project Title:** GENES THAT REGULATE ETHANOL RESPONSES IN DROSOPHILA

Abstract: A growing body of evidence is emerging from studies in animal and cellular model systems that indicates that the effects of ethanol on a variety of cellular functions are mediated by changes in specific proteins. In these systems, however, it is difficult to establish whether these proteins directly or indirectly mediate ethanol-induced changes in nervous system function. It is therefore important to establish a simple model system for alcoholism that is easily accessible to genetic and molecular analyses. We have recently initiated studies using the fruit fly *Drosophila* as a potential model system for alcoholism. Preliminary studies have shown that flies display many of the behaviors observed in humans after both acute and chronic exposure to ethanol. Flies display signs of hyperactivity and incoordination, followed by sedation and anesthesia. In addition, flies develop tolerance after single or multiple exposures to ethanol. We propose to generate and isolate *Drosophila* mutants that have altered responses to ethanol. For this purpose an "inebriometer" has been constructed, which allows the separation of flies with different sensitivity to ethanol. A genetic screen for mutants with increased or decreased sensitivity to an acute ethanol exposure will be carried out. In addition, mutant flies that fail to become tolerant or become excessively tolerant to ethanol will be isolated. Several secondary behavioral assays will be carried out to determine whether the phenotype is ethanol-specific and whether the focus of the mutation is in the central nervous system. Mutations will be mapped to specific chromosomal locations. Some of the genes affected will be isolated and sequenced. These genes will serve as tools to study molecular and biochemical mechanisms underlying ethanol-induced responses, and may in the future serve as genetic markers for alcoholism or targets for potential therapeutic intervention.

Thesaurus Terms:

Drosophilidae, central nervous system, ethanol, gene mutation, mutant alternatives to animals in research, drug tolerance, genetic regulation, genotype, mutagen, phenotype
chromosome walking, molecular cloning, nucleic acid sequence, tissue /cell culture

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Abstract

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Grant Number: 5R01EY011410-02

PI Name: HEBERLEIN, ULRIKE A.

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PI Title:

Project Title: MOLECULAR GENETICS OF DROSOPHILA RETINAL MORPHOGENESIS

Abstract: The objective of the proposed research is to understand, at the molecular level, the mechanisms underlying the early phases of retinal morphogenesis in *Drosophila*. This is a complex process by which a simple unpatterned epithelium begins to differentiate into a highly organized retina. The precision with which this developmental process is carried out is critical for achieving a fully functional visual system. Some of the molecules known to be involved in the process have homologues that are likely to execute similar functions during vertebrate retinal development. We will approach this objective by identifying novel genes, by means of a genetic screen, that carry out the various steps required for proper retinal morphogenesis. These genes should include those involved in the adoption and restriction of neural fate, in the appropriate patterning of photoreceptor precursors, and in the propagation of this pattern across the differentiating retinal epithelium. We will characterize these genes and study the phenotypic consequences of their loss and gain of function. This will be carried out by a combination of genetic, molecular, histochemical and, eventually, biochemical methods. This analysis should establish precisely what the roles of the genes are during eye development. Ultimately, these genes will provide useful tools for the process of integration, the goal of which is to establish how the various isolated components work in concert to give rise to the adult retina. Because of the emerging parallels between *Drosophila* and vertebrate eye development, we believe that the knowledge gained from this and similar studies will be applicable to the normal development of vertebrate retinae as well as to situations of genetic or environmental injury.

Thesaurus Terms:

cell differentiation, developmental genetics, epithelium, gene expression, histogenesis, regulatory gene, retina

biological signal transduction, gene complementation, gene mutation, phenotype

Drosophilidae, X ray, genetic mapping, microinjection, molecular cloning, phase contrast microscopy

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