Version 2.0

# *Abstract*

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**Grant Number:** 1Z01HD001612-02
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**PI Title:**
**Project Title:** GENETIC ANALYSIS OF RNA POLYMERASE II TRANSCRIPTIONAL REGULATION IN DROSOPHILA

**Abstract:** We are interested in understanding how genes are transcriptionally activated at the appropriate time, in the appropriate place, and for the appropriate duration during the development of complex organisms such as Drosophila melanogaster. To achieve this goal, we are using genetic approaches to identify trans-acting factors that regulate transcription of the sevenless (sev) gene, which is required for proper eye development in Drosophila. Through the expression of specific genes under transcriptional regulatory control of the sev enhancer and promoter sequences we have produced phenotypes that vary in severity in a manner that correlates with the level of expression from the sev-driven transgenes, thus creating situations in which small changes in transcription level can be detected as phenotypic alterations in adult flies. These sensitized genetic backgrounds are then used to screen for mutations that, when heterozygous, cause a change in the phenotype. For example, expression of a constitutively active form of the Ras1 GTPase (Ras1V12) under transcriptional control of the sev enhancer and promoter sequences (sev-Ras1V12) causes a rough eye phenotype that is dominantly suppressed by mutations in two TBP-associated factors (TAFs), TAF60 and TAF110. Another phenotype that is suppressed by TAF60 or TAF110 loss-of-function mutations is the synthetic lethality caused by the expression of both RasV12 and an activated form of Sev in a single fly. Presumably these transgenes act together to inappropriately activate a signal transduction pathway that interferes with proper development, and a decrease in the level of transcription from the transgenes allows development to proceed normally. We have found that this synthetic lethality is also suppressed by mutations in RNA polymerase II subunits, histone deacetylase (RPD3), and trithorax group genes. The isolation of mutations in RPD3 is in contrast to the general correlation between histone acetylation and increased transcription, and, in conjunction with trithorax group mutations, points to the importance of chromatin structure in regulating sev transcription in vivo.

**Thesaurus Terms:**
DNA directed RNA polymerase, Drosophilidae, arthropod genetics, enzyme activity, genetic regulation, genetic transcription, transcription factor

DNA binding protein, gene mutation, genetic enhancer element, genetic promoter element, guanosinetriphosphatase, intermolecular interaction
human genetic material tag, transfection

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|---|---|
| **Institution:** | |
| **Fiscal Year:** | 1997 |
| **Department:** | |
| **Project Start:** | |
| **Project End:** | |
| **ICD:** | NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT |
| **IRG:** | CBMB |