

# Requirement of Mediator complex for gene-specific transcriptional activation during *Drosophila* development

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Mediator of transcriptional regulation is the evolutionary conserved coactivator complex that plays the central role in the integration and recruitment of diverse regulatory signals and transcription machinery to certain promoters. In yeast, each Mediator subunit is required for transcriptional regulation of a distinct group of genes. In order to decipher the mechanistic roles of Mediator proteins in regulating developmental specific gene expression, we isolated, and analyzed a multiprotein complex containing *Drosophila* Mediator homologs (dMediator). dMediator interacts with several sequence-specific transcription factors and basal transcription machinery, and is critical for activated transcription in response to diverse transcriptional activators. In order to elucidate the function of Mediator in metazoan development, we isolated mutants of a conserved Mediator subunit, *Drosophila* Med6 (dMed6). dMed6 null homozygotes failed to pupate and died in the third larval instar. Larval mitotic cells and most imaginal discs showed severe defects in proliferation, but no apparent morphological defect was observed in other larval tissues. Clonal analysis of dMed6 mutant cells revealed that dMed6 is essential for cell viability and proliferation of most adult cell types. *Drosophila* cDNA microarray, quantitative RT-PCR, and in situ expression analyses of developmentally regulated genes in dMed6 mutants showed that transcriptional activation of a subset of genes involved in neuroblast proliferation in the larval brain were most affected. Our results suggest that dMed6 is required in most cells for transcriptional regulation of a subset of genes important for cell proliferation and metabolism.