Role of Motif 1 Binding Protein (M1BP), a transcriptional pausing transcription factor in JNK-mediated cell death during eye development

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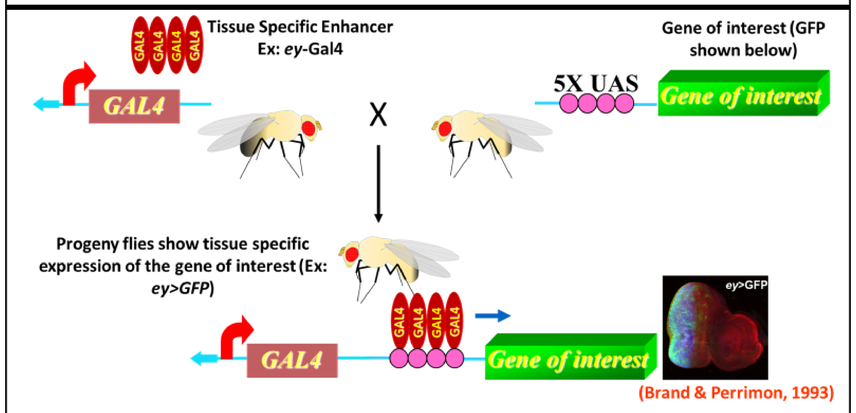
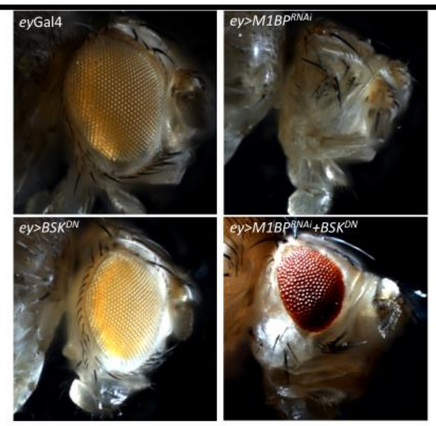
Abstract

In all multicellular organisms, transcriptional regulation is crucial to regulate differential gene expression, which is important during development and growth. Transcriptional pausing is one such mechanism used to control gene expression. Recently, we have shown that M1BP, a transcriptional pausing transcription factor, promotes eye development by suppressing *wingless (wg)* expression. We also showed that M1BP regulates caspase-mediated cell death that is triggered by wg induction. M1BP is a functional homolog of ZKSCAN3, an autophagy repressor in humans. Jun-amino-terminal-(NH2)-Kinase (JNK) signaling is a pro-death pathway that is known to activate caspase-mediated cell death. We hypothesize that M1BP could have a role in mediating cell death via JNK signaling during eye development. In our studies, we explore the modulation of JNK signaling and its effect on M1BP mediated cell death by using the GAL4-UAS system. We present preliminary data that shows that the absence of M1BP function results in activation of autophagic cell death markers and JNK signaling.

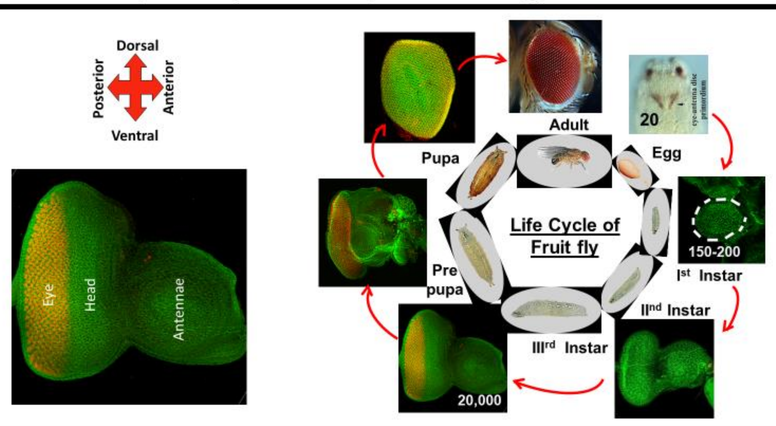
Gal4-UAS System



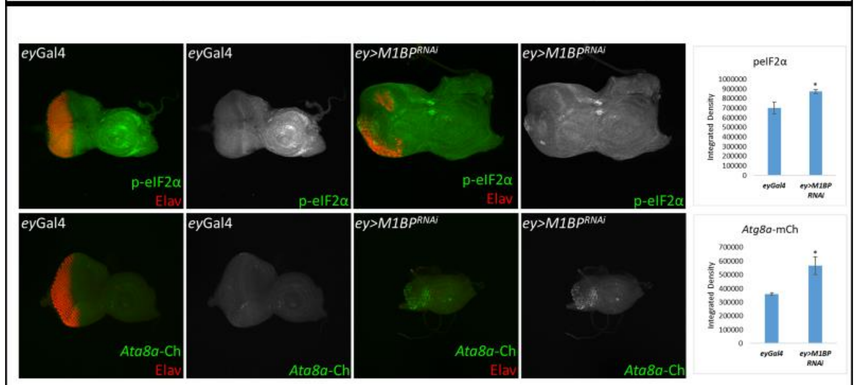
Downregulation of JNK pathway rescues eye suppression by M1BP^{RNAi}



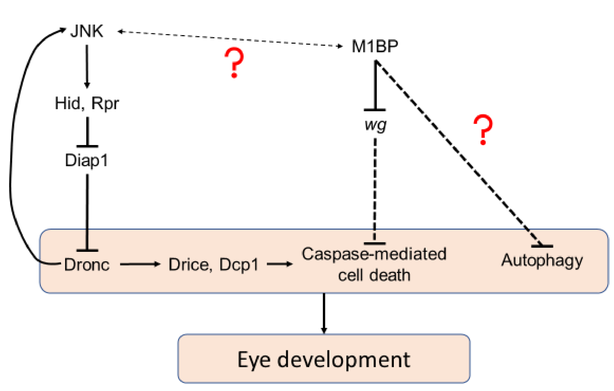
Drosophila eye development along the time axis



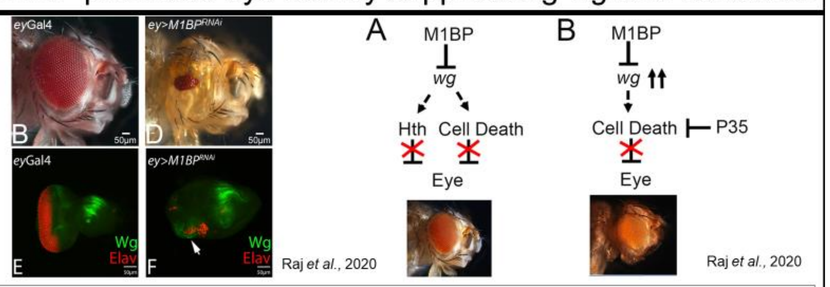
Downregulation of M1BP induces autophagic markers



Role of M1BP^{RNAi} and its interaction with JNK signaling during eye development



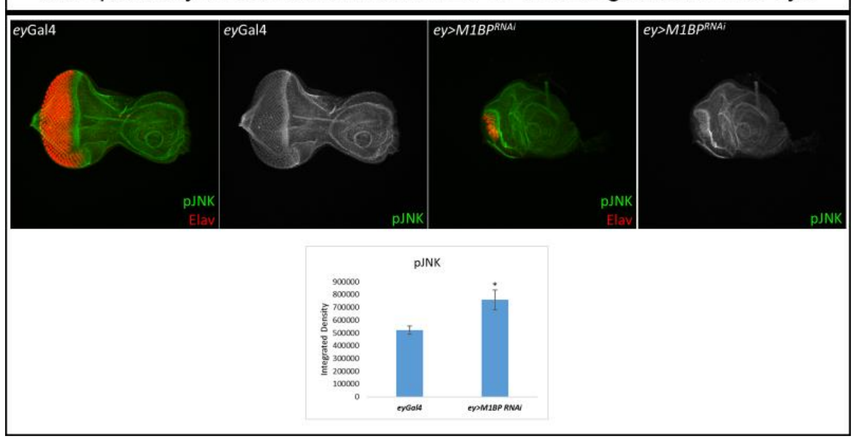
M1BP promotes eye fate by suppressing *wg* and cell death



Downregulation of M1BP induces *wg* and apoptotic cell death.
Inhibition of caspase-dependent cell death using p35 shows significant but incomplete rescue.

1. Does autophagy, another form of cell death, have a role during eye development?
2. Does JNK pathway, a proapoptotic pathway interact with M1PB during eye development?

JNK pathway is activated when M1BP is downregulated in the eye



Conclusions and Future directions

Conclusion

- Downregulation of M1BP induces autophagy (increased peIF2α and *Atg8a*-mCh) and JNK pathway (pJNK) during eye development
- Downregulation of JNK pathway can rescue the *ey*>M1BP^{RNAi} eye suppression phenotype suggesting that M1BP may interact with JNK pathway to regulate cell death during eye development.

Future directions

- Modulate other components of JNK pathway and see how it interacts with M1BP
- Check how autophagy is regulated by M1BP and if blocking autophagy can rescue eye suppression.

We thank Bloomington Drosophila Stock Center (BDSC) for Drosophila strains, and the Developmental Studies Hybridoma Bank (DSHB) for antibodies. This work was supported by start-up research funds from the University of Dayton, NIH1R15GM124654-01 from NIH, Schuellein Chair Endowment Fund and STEM Catalyst Grant from the University of Dayton to A.S.