Genetic analysis of spermatogenesis and aging in *Drosophila*

**Abstract:**
Although many theories of aging abound, the underlying molecular mechanisms of aging are still unknown. Molecular aging clocks provide insights into the molecular changes occurring during the aging process. We cross referenced human epigenetic and blood aging clocks with transcriptome trajectory turning point genes from brain data to identify 3 genes (Loxl2, fz3, and Glo1) that positively affected lifespan when inhibited in *Drosophila*. Furthermore, knockdown of Loxl2 was able to prevent cardiac arrhythmia and reduce fibrotic markers (collagen thickness) with age. We showed that Loxl2’s transcriptional regulatory functions in mammals are likely conserved in *Drosophila* as RNA levels of the cadherin CadN2 correlated with Loxl2 reduction in flies. These results single out Loxl2 as an important molecule in cardiac and organismal aging and identify several pathways through which the benefits of Loxl2 reduction are likely derived.

Aging in *Drosophila* accompanies a decline in total RNA concentration, but the mechanisms behind this decline have yet to be discerned. Proper transcription factor levels, and subsequent localization to the nucleus, are required for the regulation of RNA concentration. Therefore, establishing which transcription factors have reduced nuclear access with age is an important step in determining why decreased gene expression occurs with age. To begin to examine this question we fractionated the nuclear from the cytoplasmic contents of *Drosophila melanogaster* whole flies and examined protein identity, quantity, and localization with age using western blots and plan to further expand on these results using Tandem Mass Tag Labeling Mass Spectrometry. We found that the transcription factor SMOX had reduced nuclear localization with age, revealing that nuclear localization of transcription factors may play a role in the decline of transcription with age in *Drosophila*. 