

# The Effects of Heart-Specific Downregulation of Histone Deacetylase, Rpd3, on Longevity

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Extensive studies have been done on the causes and consequences of aging, but the actual mechanism behind this process is only partially understood. My research on Rpd3, a homologue of mammalian Histone Deacetylase (HDAC1), aimed to elucidate the longevity mechanism using *Drosophila melanogaster* as the model organism. Recent research has shown that systemic downregulation of Rpd3 extends lifespan in fruit flies, while heart-specific Rpd3 downregulation enhances cardiac function and stress resistance. In this project, I investigated whether Rpd3 downregulation in the heart would extend longevity. Using the UAS-Gal4 system and RNA interference to downregulate Rpd3 in the heart by 70%, aging assays were performed. The results demonstrate that lifespan was extended up to 40% in flies with heart-specific Rpd3 downregulation compared to the control, or non-specific Rpd3 downregulation ( $p < 0.0001$ ). Subsequently, in order to characterize the genes that function in the heart-specific Rpd3 longevity mechanism, gene expression profiles in heart-specific Rpd3-downregulated young (1-week-old) and old (7-week-old) flies were compared. Genes that showed commonly changed patterns in expression level were further analyzed. RT-PCR was used to confirm four candidate genes that showed more than two-fold changes in differential expression at both young and old ages. Next, tissue-specific expressions of the candidates were compared, and CG14957 and CG13155 displayed heart-specific expression changes with Rpd3 downregulation in the heart. This suggests that Rpd3 may regulate secreted proteins from these target genes to systemically modulate longevity.

## Awards Won:

Third Award of \$1,000