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.

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Third Award of $1,000