The Effect of Circadian Genes dbt and bdbt on the Lifespan of Drosophila melanogaster

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The circadian clock regulates human activities; it can affect the well-being of individuals, including their life expectancy. Doubletime (DBT) is an ortholog of mammalian casein kinase which regulates various cellular functions, including circadian clock and cell cycle. CG17282 Bride of DBT (BDBT) is a newly identified protein associated with DBT; it may also be related to life expectancy. It was hypothesized that flies with wild type DBT and BDBT protein levels will live the longest because the flies have the most robust circadian rhythms and do not activate cell death pathways. Flies in which dbt and bdbt had been knocked-down in clock cells were assessed for lifespan and activated caspase (a marker of cell death). 30 male and female flies of each genotype were separated. Every three to four days the amount of living flies was recorded. At three days, one week, and two weeks, heads were removed from some of the flies, and used for protein extracts and subjected to a Western blot analysis of apoptotic markers. The Canton S (wildtype) control flies had the longest lifespan out of the three genotypes. The other two groups, dbt knocked-down flies and bdbt knocked-down flies had shorter lifespans, although the bdbt RNAi flies outlived the dbt RNAi flies in the first experiment but not the second one. Intriguingly, mutant male flies tended to die sooner than mutant female flies, and activated caspase was detected 3-days after collection only at ZT7 (middle of the day) in dbt RNAi male flies, which had the shortest lifespan. Activated caspase was not detected in older flies, suggesting that activation of the caspase may contribute to subsequent shortened lifespan. The activation specifically at ZT7 suggests a link between altered circadian function and shortened lifespan.

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