Genetics Day Poster Submission

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Category: Other

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Title: THE FUNCTION OF HEAT SHOCK FACTOR IN DROSOPHILA DEVELOPMENT

Abstract: Heat Shock Factor (HSF) is a transcriptional factor that is conserved from yeast to mammals and is recognized as the master regulator of the stress response. When eukaryotes are exposed to high temperatures or other stresses, HSF transcriptionally activates a family of molecular chaperones called Heat Shock Proteins (HSPs) to refold damaged proteins. However, in recent years, HSF has been found to have noncanonical functions beyond stress responses. It has been shown to play an indispensable role in promoting carcinogenesis and tumor progression in mammalian tumor models and cultured cancer cells by regulating pro-cancer genes. It also promotes non-apoptotic linker cell death in C. elegans by activating a ubiquitin-proteasome system and is essential for the early development of C. elegans by regulating developmental genes. The diverse roles of HSF raise the central question of how this transcriptional factor regulates different sets of genes under different conditions. To answer this question, we used Drosophila melanogaster as a model system. We probed HSF's function in Drosophila tissue growth, as the literature suggested that HSF null larvae die at an early developmental stage when massive proliferation and growth occur. Using the UAS-Gal4 system, we performed tissue-specific knockdown of HSF. Salivary gland secretory cells showed reduced nuclear and cell size after the knockdown. Knockdown in larval wing discs led to defects in adult wings. Less HSF in the germline caused degenerating egg chambers and embryo lethality. These results suggest that during normal development HSF is required for both cell growth and cell proliferation. Interestingly, knockdown of HSF in the prothoracic gland (PG), an organ that synthesizes the hormone ecdysone, caused larvae arrest at the third instar stage without pupariation. The arrest was rescued by raising the animals on ecdysone-containing media, suggesting that those larvae cannot produce enough ecdysone. The ecdysone production requires PG to reach a certain organ size by endoreplication and cell growth. We dissected the HSF knockdown PG and found it was smaller in both organ size and nuclear size than the wild type, suggesting there were defects in endoreplication and growth. Since Hsp83 is an essential molecular chaperon regulated by HSF at non-stressed conditions and is highly expressed in the PG, we tested if our PG phenotype is caused by a downregulation of Hsp83. We restored Hsp83 expression in the HSF knockdown PG, and it rescued both the arrest phenotype and PG size to the wild-type level, suggesting that HSF promotes PG growth by regulating Hsp83 expression. We are currently studying how Hsp83 regulates PG growth and whether other HSF knockdown phenotypes can be explained by a similar downregulation of Hsp83.