

IMMUNE FUNCTION, ENERGY METABOLISM AND AGING IN DROSOPHILA

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A common observation in the aging human population is a gradual increase in visceral fat between the third and fifth decades of life. An accumulating body of evidence suggests that visceral adiposity is also associated with low-grade inflammation characterized by abnormal production of cytokines and other stress-induced molecules. Genetic studies in model systems have shown that mutations in genes involved in insulin/IGF-like signaling (IIS) extend life span. Reduced IIS has also been associated with fat accumulation in *Caenorhabditis elegans* and *Drosophila melanogaster*. Moreover, long-lived *C. elegans* mutants of the IIS pathway have been shown to be resistant to bacterial pathogens and may exert their effect on life span by up-regulating a wide variety of genes, in particular antimicrobial and metabolic genes. These findings suggest that evolutionarily conserved genetic pathways regulate age-related changes in triglyceride storage and innate immune function through common regulatory molecules. We are exploring this hypothesis using a quantitative genetic approach and *D. melanogaster* as a model system. Both triacylglycerol storage and innate immune response are complex polygenic traits, influenced by a large number of genes (Quantitative Trait Loci or QTL) and the environment. Therefore, a quantitative genetic approach offers promise for identifying loci that contribute to natural variation in these traits and estimating the relative effects of these loci across genetic backgrounds and different environments. *D. melanogaster* is being used as a model system because genetic mapping procedures are well-developed for this species. *Drosophila* is also an excellent model to explore the genetic interrelationship between fat metabolism and antimicrobial defense because both of these functions are largely carried out by the fat body, the functional equivalent of the mammalian white adipose tissue and hematopoietic/immune organs. Preliminary results will be presented and discussed.