Innate Immune System Involvement in Brain Tumor Formation in Drosophila melanogaster Brat Mutant: A Research Model of Pediatric Brain Tumor Development

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Abstract

The innate immune system is a critical first-responder line of defense coordinating in *situ anti*-cancer responses with adaptive immune system regulation. Research in my laboratory on brain tumor development in pediatric patients involves the use of a strain of the model organism, *Drosophila melanogaster*, that contains a temperature-sensitive mutation in the brain tumor suppressor gene "*brat*". The abnormal brat protein causes the formation of brain tumors that resemble human brain tumors, both genetically and physiologically, including analogs of human innate immune system genes and the brat tumor suppressor gene, which is an analogue of the human ortholog TRIM3.

Drosophila does not possess an adaptive immune system; its innate immune system (which bears many similarities to its human counterpart) is the focal point of its anti-tumor immune responses. This fundamental difference in immune system complexity facilitates a direct assessment of this tumor/immune system interface that is the driver of more complex adaptive immune responses in humans. The research involves comparative assessment of the innate immune system profile in each stage of tumor development in *brat* activated *Drosophila* embryos and larvae as compared to their levels in normal central nervous system development in the fly. This work involves live tissue imaging studies of dissected central nervous system tissues from *Drosophila* at each stage of development in normal versus brat mutant flies, in which brain tumor formation occurs as a consequence of dysregulated brain development, in many ways replicating patterns of pediatric brain tumor development in humans.

This inquiry also involves analyzing the hemolymph immune system components at each stage of normal versus malignant central nervous system development. In addition, embryonic cell cultures are assessed *in vitro* with respect to the effects of innate immune system components on their growth patterns and properties. These embryonic stem cells, derived from Drosophila embryonic tissue, allow a precise characterization of the cellular effects of abnormal immune system components produced by larval flies during tumor development on growth of cells under conditions where these cells may display altered growth rates as well as abnormal patterns of growth in the context of the immune system components derived from flies with incipient brain tumors. This research presentation will identify critical innate immune system parameters during early-stage tumor development that may contribute to immune system repression and the failure to control tumor growth.