ABSTRACT

ANALYSIS OF GLIA-NEURON INTERACTION AND CELL DEATH PATHWAYS IN *DROP-DEAD* MODEL OF ADULT NEURODEGENERATION

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Adult neurodegeneration is one of the main reasons for early death in the global elderly population. The connections among glial cell morphology, immunity, and neurodegeneration are underexplored. Here we present a *Drosophila melanogaster* gene *drop-dead* (*drd*) as a unique model to study glial ND.

drd affects brain glial morphology while being expressed in the tracheal processes adjacent to the brain cells. The cortex glial network houses all neuronal cell bodies in flies and helps neurons to perform crucial cellular functions. Breakdown of this network and early apoptosis are the primary *drd* neurodegeneration phenotypes. As a result, the mutant brains have a significantly smaller number of live cells.

The broken cortex glial network harbors the majority of apoptotic cells with significant variations among individual brains. The lack of the glial network around the neurons can result in widespread cell death. The primary *drd* neurodegeneration phenotypes start early in adulthood and are followed by secondary cell death mechanisms such as hyperactivation of all immune markers AMPs and subsequent oxidative stress induction. We performed preliminary experiments to identify the mechanisms of neurodegeneration facilitated by CG network breakdown.

Overall, *drd* mutant model provides new insight to study ND by displaying altered neuron-glia interaction, and age-dependent activation of apoptosis, immunity, and oxidative stress.