Project title: Role of E2 conjugating enzyme effete-UbcH5b in DNA repair and neuroprotection

Partners:

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Description:

The reduced efficiency of DNA repair mechanisms is linked to several aspects of neurodegeneration. Ubiquitination is a post-translational modification required for protein degradation and regulation. Alterations in this process are associated with many pathologies, including cancer and neurodegeneration. The *Drosophila effete* (*eff*) gene encodes UbcD1, a conserved E2 conjugating enzyme involved in apoptosis, development, genome stability, chromatin organization and telomere protection. The project aims to understand the role of UbcD1 in the maintenance of genomic integrity and physiology in neuronal cells.

Aims:

The specific tasks are designed to verify whether *eff* and its human ortholog *UbcH5b*, functionally interact with DNA Damage Response (DDR) pathways components to preserve neuron viability and function. To this aim, we will assess the effect of *eff*/*UbcH5b* depletion in flies and mouse motor neuron like cells (NSC-34) on viability, differentiation and functional activities. Then, we will analyze genetic interactions between *eff* and DDR encoding genes and their effects on neuronal homeostasis.

Expected results:

The results from this study will deepen our understanding of the role of ubiquitination in genome stability maintenance of neurons. Moreover, the *Drosophila* model of *eff*-dependent neurodegeneration will elucidate conserved mechanisms underlying neuroprotection at the whole organism level. Since neuronal death in neurodegenerative diseases derives from misfolded protein aggregation, our animal model will be instrumental to further analyze protein turnover through degradation in brain homeostasis.

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