In vivo and in vitro Drosophila models to study the role of heparan sulfate in Alzheimer´s disease pathogenesis

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In vivo and in vitro Drosophila models to study the role of heparan sulfate in Alzheimer´s disease pathogenesis

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Research Abstract

Alzheimer´s disease (AD) is the most common form of dementia that disrupts memory, thinking and behavior. Neuropathological hallmarks of AD include extracellular amyloid plaques that are primarily composed of Amyloid- peptides (A). A is a heparin/heparan sulfate (HS)-binding protein, and HS affects multiple aspects of AD pathogenesis. HS is a linear polysaccharide that binds to a variety of protein ligands and regulates a wide variety of biological activities, such as

growth factor signaling, cell adhesion, and enzymatic catalysis. However, the mechanisms by which HS affects A deposition, internalization, and clearance, remain to be elucidated. Since HS modifications (such as sulfation) have a major impact on HS function, it is critical to define how HS modifications affect each step of AD pathogenesis. We propose to address this question using the Drosophila model. Drosophila genetics has been used for AD research, and we have established the Drosophila model as an excellent system to study in vivo functions of HS. A current obstacle for Drosophila HS research is the difficulty of determining higher order structures of HS. To overcome this, we propose to establish Drosophila cell lines mutant for these enzymes. Once cell lines are established, in vitro and in vivo analyses in Drosophila can be performed in parallel, which provides an extremely powerful platform to study the roles of HS in AD conditions. The hypothesis to be tested is that specific HS fine structures play critical roles at different steps of AD pathogenesis. This project will thus provide a knowledge foundation for the future development of AD treatments and therapies.

Further information available at:

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