CALIFORNIA STATE SCIENCE FAIR
2002 PROJECT SUMMARY

Name(s)

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Project Number

22607

Project Title

Age and Lesion-Induced Changes in Protease Nexin 1 Expression in the Brain

Abstract

Objectives/Goals

The blood brain barrier is an important structure in the maintenance of brain homeostasis. Protease nexin 1 (PN1) is a 43-kDa serine protease inhibitor (serpin) found predominantly in the brain. Secreted by a variety of glial cells, PN1 concentrates around blood vessels and capillaries to inhibit blood-borne thrombin. Extravasation of thrombin due to blood brain barrier compromise has been shown to be remediated by potent PN1 inhibition. PN1 activity clears thrombin, and promotes neuritic outgrowth vital in nervous system development and repair processes. The present study was designed to test the hypothesis that PN1 concentrations after injury are increased, while decreased with brain aging.

Methods/Materials

For these experiments, two methods of analysis will be employed. In the first experiment, immunocytochemistry will be used to compare the expression of PN1 in brains with ibotenic acide lesions that simulate brain injury. In the second experiment, immunocytochemistry will be used to compare intensity of PN1 staining in aged vs. young rats. In the third experiment, Western Blot analysis will be used to quantitatively compare expression of PN1 in aged vs. young rats.

Results

In the first study, rat brains with ibotenic acid lesions simulating injury in the brain were stained to verify the expression of PN1. Results of this immunocytochemical staining illustrated strong differences in PN1 expression at sites of injury, revealing an increase in response to brain damage. In the second study, PN1 concentrations were quantified in aged (over 24 months) and young (3 months) rat brains. Protein quantification assays carried out by Western blot revealed a decline in PN1 expression relative to age.

Conclusions/Discussion

These results suggest that PN1 levels could be tied to the decline in neuronal protection that accompanies memory loss, senile dementia, and neurodegeneration. PN1 has already been evidenced to contribute to the pathology of Alzheimer's disease, and it may be of interest to further explore its role in neuronal protection. The possibility of its use in therapeutics is also worth pursuing.

Summary Statement

This project hopes to elucidate the roles of protease nexin 1 in aging and protecting the brain against injury that may arise from trauma or neurodegenerative disorders.

Help Received

Worked under the supervision of Sonsoles de Lacalle at the California State University, Los Angeles.