

Summer Student Research Program
Project Description

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PROJECT TITLE (200 Characters max):

Mechanisms of neurodegeneration and neuroprotection in animal models of multiple sclerosis

HYPOTHESIS:

Neuronal injury and death in an animal model of multiple sclerosis may be the result of excitotoxicity-induced reductions in plasma membrane calcium ATPase 2 (PMCA2), a neuronal calcium pump, and collapsing response mediator protein 1 (CRMP1), a protein that plays critical roles in the assembly of the cytoskeleton.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

It is now well accepted that neuronal injury and loss occur at early stages of multiple sclerosis (MS) and are major determinants of permanent deficits. Yet, little is known about the mechanisms underlying neuronal damage. Delineation of such mechanisms is essential for the identification of novel therapeutic targets.

The Elkabes laboratory has found that a reduction in PMCA2 causes a decrease in CRMP1 which is followed by neuronal death. Both PMCA2 and CRMP1 levels are reduced at onset of symptoms during experimental autoimmune encephalomyelitis (EAE), an animal model of MS. Restoration of PMCA2 and CRMP1 levels coincides with amelioration of symptoms after treatment of affected mice with a glutamate receptor antagonist. The interactions between PMCA2 and CRMP1 and the modulation of such interactions during EAE have not been defined and will be the focus of the current project.

EAE will be induced by immunization of mice with a peptide derived from myelin oligodendrocyte glycoprotein and the development of motor deficits will be evaluated. Approaches such as immunoprecipitation, western blots, gene expression silencing by use of siRNA and neuronal cultures will also be used.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

Kurnellas MP, Li H, Jain MR, Giraud SN, Nicot A, Ratnayake A, Heary RF, Elkabes S. 2009 Reduced expression of plasma membrane calcium ATPase 2 and collapsin response mediator protein 1 promotes death of spinal cord neurons: relevance to neurodegeneration in autoimmune encephalomyelitis. In revision for Cell Death and Differentiation.

Kurnellas MP, Donahue KC, Elkabes S. 2007 Mechanisms of neuronal damage in multiple sclerosis and its animal models: role of calcium pumps and exchangers. Biochem Soc Trans. 35:923-6.

Kurnellas MP, Nicot A, Shull GE, Elkabes S 2005 Plasma membrane calcium ATPase

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deficiency causes neuronal pathology in the spinal cord: a potential mechanism for neurodegeneration in multiple sclerosis and spinal cord injury. FASEB J. 19:298-300. Epub 2004 Dec 2.

IS THIS PROJECT SUPPORTED BY EXTRAMURAL FUNDS?

Yes or No

(IF YES, PLEASE SUPPLY THE GRANTING AGENCY'S NAME)

NIH-NINDS

THIS PROJECT IS: Clinical Laboratory Behavioral
Other

THIS PROJECT IS CANCER-RELATED

Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED

Please explain Heart, Lung, Blood relevance

THIS PROJECT EMPLOYS RADIOISOTOPES

THIS PROJECT INVOLVES THE USE OF ANIMALS

PENDING APPROVED IACUC PROTOCOL #
08101E1111

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS

PENDING APPROVED IRB PROTOCOL # M

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS ENTERING FRESHMAN
SOPHMORES ALL STUDENTS

THIS PROJECT IS WORK-STUDY: Yes or No

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR

FOR INTERESTED VOLUNTEERS?: Yes or No

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?

Some of the principles and mechanisms underlying neurodegeneration and neuroprotection in multiple sclerosis.

Induction of experimental autoimmune encephalomyelitis, an animal model of MS.

Behavioral analysis of motor function.

Tissue culture and molecular techniques.

Data analysis and interpretation of results.