

## Steven R. Sawyer Memorial Research Award Summer 2009

Project Title: Affinity-Based Isolation from Brain Cells and  
Identification of Candidate Redox Receptor Proteins

Project Mentor: Tim Foley, PhD; Associate Professor of Chemistry

Eligible Applicants: Pre-medical, pre-dental or pre-veterinarian students in  
the classes of 2011 and 2012; should be active members  
of the Health Professions Organization

Application due: March 30, 2009

Submit to Michele Langan, Biology Department Office, Loyola 115

Research stipend: \$3,500.00

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### **Background**

Oxidation-reduction (redox) reactions play central roles in the daily lives of cells. While the inside of cells is normally a highly reducing environment, increases in the production of O<sub>2</sub>-derived cellular oxidants beyond the capacity of antioxidant systems to remove them sufficiently leads to a state of "oxidative stress". There is great interest in understanding the biochemical pathways by which cells respond to oxidative stress as this state is implicated strongly in the onset and progression of aging-related diseases including Alzheimer's disease, heart disease, and certain cancers. Mounting evidence suggests that specific and reversible oxidization of reactive cysteine thiols (-SH) on ill-defined regulatory proteins, which have been termed "redox receptors", may underlie key responses of cells to oxidative stress. Thiol oxidation-based changes in the function of these redox receptors produce secondary changes in metabolism and gene expression leading to alterations in cellular activity. A complete understanding of the cellular responses to oxidative stress will require identification of the redox receptor proteins.

Isolation of proteins that undergo reversible oxidation of cysteine thiols presents challenges due to the ease of reversal of these changes produced by reducing agents that are usually included in biochemical experiments. Recent work in Dr. Foley's lab has centered on the development of chemical methods to trap proteins from rat brain extracts that undergo reversible oxidation of thiols so that these may be separated from unoxidized proteins and identified. Thus, students in Dr. Foley's lab have succeeded very recently in capturing proteins that undergo selective oxidations in vitro to form intraprotein disulfide bonds (-S-S-) and mixed disulfide bonds with the tripeptide antioxidant glutathione. Key proteins that are most selectively oxidized from among the

total population of the brain extract proteins have been identified by mass spectrometry and by the use of antibodies to include the synaptic protein SNAP-25, which is involved in neurotransmitter release, and triose phosphate isomerase, which is an enzyme involved in glycolysis.

**Research**

Work by students in Dr. Foley’s lab this summer will be directed at (i) identifying additional redox receptor proteins, (ii) developing an intact cell model so that oxidation of the candidate redox receptor proteins identified in the brain extracts can be tested in a more physiologically-relevant system, and (iii) examining the functional significance (e.g., effect on enzyme activity) of the oxidation of the candidate redox receptor proteins.

**Schedule**

The award recipient will be expected to devote to the project an average of 40 hours/week for 10 weeks during the summer of 2009.

**Qualifications**

Interested students should have an interest in biomedical research and a strong academic record. Preference will be given to students who have an interest in pursuing a long-term research project.

**Student Application**

Name \_\_\_\_\_

Address \_\_\_\_\_

Phone \_\_\_\_\_ email: \_\_\_\_\_

Major(s) \_\_\_\_\_ GPA \_\_\_\_\_

Other Curricular Programs in which you take part (e.g. Honors, SJLA, FSRP) \_\_\_\_\_

Expected Graduation Date \_\_\_\_\_

Biology/Chemistry/Laboratories/Honors Tutorial Courses Completed (please indicate grade received in parentheses) or In Progress \_\_\_\_\_

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Brief Description of Involvement with/Contribution to the Health Professions Organization

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Brief Description of Volunteer Activities

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Research Experience (please briefly describe the project, the duration of your participation, and your progress to date) \_\_\_\_\_

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What is your interest in participating in *this* summer research project? \_\_\_\_\_

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Describe your course and/or research experience that is most relevant to this research project.

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Are there any special circumstances that would make this research award particularly helpful to you? \_\_\_\_\_

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Goals/Plans for the future \_\_\_\_\_

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Other Comments \_\_\_\_\_

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