IEH Undergraduate Intern Mentoring Opportunity

Deadline: **February 22, 2013**
Selections Announced: **mid-March, 2013**

Name/Title/Institution(s) of senior mentor(s):

Chelsey Kline, Graduate Research Student, Oregon Health and Science University

Mary Mayfield, Research Associate, Oregon Health and Science University

Name/Title/Institution(s) of frontline mentor(s):

Ninian Blackburn, PhD Professor, Oregon Health and Science University

Project Title:

Coordination of Cu (I) binding in the ATP7A HM loop is modulated by pH

Context for Project:

Copper proteins (PHM and DBM) require metallation performed by copper transporting ATPases (ATP7A and/or ATP7B) within vesicles containing a relatively low pH (~5.5). It is believed that copper is directly transferred from the ATPase to their putative partner, but release of copper is not well understood. Recently there have been two major findings: 1) ATP7A contains a lumenal loop rich in histidines and methionines found to bind Cu (I) but is not structurally conserved in ATP7B (possibly providing differences in their ability to transport copper); 2) PHM contains a histidine, histidine, methionine (HHM) motif that is a pH-dependent conformational switch. It is believed that the "HM Loop" binds copper as it is released from the transmembrane binding sites and transfers it to copper proteins like PHM, which are both subject to the vesicles low pH environment. At present, the pH-dependence on Cu (I) binding coordination has not been investigated in the HM loop, and is required in order to provide insight into the mechanism of copper release.

Brief Description.

During the internship, we will be using mutagenesis in combination with spectroscopic tools to probe the pH-dependent Cu (I) coordination of the HM loop. This will provide insight into the structure and function relationship required for copper trafficking in cells.

Proposed Outcomes/Broader Impact:

The proposed research will not only promote teaching experiences otherwise not possible for graduate research students at this institutes location, but also the ability for an undergraduate student to learn about biochemical research first hand. This research will include using novel SeM labeling (pioneered in the Blackburn lab) in conjunction with X-ray Absorption Spectroscopy (XAS) at the Stanford Synchrotron Radiation Lightsource (SSRL) facility to use as a spectroscopic probe for Cu (I) coordination where other

spectroscopic probes are absent. The integration of education and research expands the participation in multiple scientific institutions, which would allow us to advance the understanding of human diseases.

Proposed timeline (within a 10 week span):

All 10 weeks will be utilized.

The first three weeks will be used to make and produce multiple mutant proteins.

The next three weeks will be used for protein purification.

The last three weeks will be used to spectroscopically characterize each mutant at various pHs.

(One extra week is allocated for anything that could go wrong, as well as for making posters, and teaching.)

Intern academic experience and skill set should include:

I prefer students who have an interest in biochemistry, chemistry, and/or biology. I would like to work with a more experienced candidate.