Example of a Well-Written Research Proposal: Basic Science Project

Please note: The following proposal was written by a student who was accepted into the research program for summer 2005. The format is slightly different than what is required for the summer 2006 application.

B. Project Description

a. Project Title

Metabolic Effects of Amyloidogenic κ1 Light Chain Internalization and Localization

b. Description/Goals of Project

Amyloidosis is a family of diseases characterized by aggregations of misfolded proteins throughout the body. Some forms of amyloidosis include Alzheimer's disease, Parkinson's disease and systemic (AL) light chain amyloidosis. Investigators of the mechanisms of amyloidosis are just now beginning to get a brief glimpse of how the diseases begin and progress in the human body. Amyloid fibrils appear in different tissues throughout the body, including the heart, which is the most commonly affected organ in AL amyloidosis. Since AL fibrils are believed to be composed of fragments of immunoglobulin light chain proteins that are found natively in the body, it is hypothesized the immune system produces excess light chain which is internalized by cells, processed, and then exported to the extracellular milieu where the fibrils form by an unclear mechanism. The current thrust of research in the Trinkaus-Randa11 Lab is to understand how the light chain is internalized and processed within the cells before it is exported. Preliminary results indicate the light chain is cycled between the cell and the extracellular environment. More results also suggest subcellular localization patterns, including the nucleus and perhaps the Golgi apparatus. Further curious data have suggested the light chain is actively mobilized within the cell, perhaps along cytoskeletal structures. The primary goal of my project will be to further elucidate specific subcellular localization patterns of light chain and to begin to understand whether light chain affects cell metabolism by studying changes in gene transcription.

c. Hypotheses being tested

i. 00131 κ1 light chain localizes to the Golgi apparatus.
ii. 00131 κ1 light chain localizes to various structures within the endosomal and lysosomal pathways.
iii. 00131 κ1 light chain modifies gene transcription as determined by histone acetyl transferase assays.
iv. 00131 κ1 light chain is transported along actin fibers and/or microtubules
v. l00131 κ1 light chain localizes to the nucleus.

d. My Role

Because of previous work experience using a confocal microscope, Dr. Trinkaus-Randall has allowed me to perform my work primarily by studying the light chain using microscopy. My role will be to assist in culturing primary rat cardiac fibroblasts that I will treat with light chain. The cells, once treated with fluorescently-tagged light chain may be fixed and further stained to visualize other structures via fluorescence, such as Golgi or actin. I have also developed an imaging protocol to obtain movies of live cells that have been treated with fluorescent light chain in order to develop a kinetic model of movement of light chain throughout the cell. I will also work closely with the technician and MD/PhD student who are also actively involved with amyloid research in the lab in order to develop a global picture of internalization, localization and any metabolic changes elicited by light chain.

e. Research Techniques I will learn

As I have already been trained on the techniques I will be using, additional training will not be required. However this project will afford an excellent opportunity to learn a new technology Dr. Trinkaus-Randall has just acquired, a pico-spritzer, which will hopefully allow me to study individual live cells that have been "spritzed" with a light chain solution, which will ideally benefit live cell imaging, as it will alleviate problems associated with background fluorescence, which is a current problem with my model.

f. My supervisor

Dr. Trinkaus-Randall will supervise me.

g. Status of Project

I worked for Dr. Trinkaus-Randall year to perform work that led to a MA Medical Sciences thesis. This project is a continuation of that work. I have recently begun working in her lab again and expect to continue to do so over the course of the summer in order to produce a publication describing my investigation.