

**Division of Biological Sciences
Honors Research (BioSc 4950H) Application**

Your Name: John Smith

Mentor's Name: Jane Doe

Mentor's Department: Biological Sciences

Title of Project: Cell Death within an *in vitro* model of a neural stem cell niche

Background Information on Project: Stem cell therapies have the potential to treat neurodegenerative diseases, such as Parkinson's disease and Batten disease. Batten Disease, a rare inherited disease in children, causes severe neurodegeneration, which results in blindness, seizures, and premature death. In Batten disease, the transplantation of stem cells into a patient may replace lost cells or prevent cell loss due to the disease. In one form of Batten disease, transplantation of stem cells into the retinas of mutant model mice have shown signs of neuroprotection, including enhanced survival of photoreceptors (Meyer et al. 2006). One possible method to increase the efficiency of this treatment is the transplantation of a functional unit capable of producing its own neural precursors "on demand." Such a structure, known as a neural stem cell (NSC) niche, can be found in two small areas in the brain of mammals, and is the center for adult neurogenesis throughout the lives of these animals.

Experimental Approaches: Our lab has developed a way to produce an NSC niche-like structure *in vitro* from neuralized mouse embryonic stem cells. To test how this structure is formed and maintained, I am investigating cell death within this *in vitro* NSC niche-like structure. I will perform two different tests for apoptosis or programmed cell death, Trypan Blue exclusion and TUNEL. Trypan Blue shows membrane permeability; if cells turn blue (Trypan Blue is not excluded) it is indicative of a late stage in the apoptotic process. In the TUNEL assay, nicked ends of DNA are labeled, an indication of early stage apoptosis. I also will test the effects of induced cell death on the advancement of *in vitro* niche formation.

Predicted Outcomes: Many cells in the cultures may differentiate and not survive the minimal culture media used to generate the NSC niche-like structures. If this prediction is true, differentiated cells with complicated morphologies will exhibit Trypan Blue and TUNEL labeling. We predict that the labeled cells will also label for mature neural markers, such as neurofilament and NeuN, indicating the sensitivity of highly differentiated cells to the culture conditions.

Overall Significance: These experiments will test whether programmed cell death contributes to formation of NSC niche-like structures *in vitro*. Future studies will focus on signaling events that occur in the cultures that are required for niche formation. We hope that this information will lead to a better understanding of how the *in vitro* niche forms and will provide new methods for stem cell transplantation and enhanced clinical applications of stem cell therapies.

Cited Literature:

1. Meyer, JS, Katz, ML, Maruniak JA, and Kirk MD. 2006. Embryonic stem cell-derived neural progenitors incorporate into degenerating retina and enhance survival of host photoreceptors. *Stem Cells* 24, 274-283.