Project Description

In the event that I am given the opportunity to initiate a research project under the direction of Dr. Albert Magro, the cells to be used in my experiments will be the LN-18 glioblastoma obtained from ATCC (cell strain CRL-2610). The interest in glioblastomas stems from the fact that this type of malignancy is very invasive and is nearly 100% fatal. Chemotherapeutic regimens for glioblastomas and other high grade gliomas have fallen short of providing effective treatment. Clinical studies comparing chemotherapeutic agents have indicated increased tumor shrinkage and a very slight increase in median survival times, but no evidence for an increase in survival rates [1]. More recent clinical studies using chemotherapeutic regimens either in combination with radiation therapy [2] or in combination with gene silencing regimens [3] are slightly more effective in increasing median survival times, but again have had limited success in increasing the overall survival rate in patients being treated for primary or recurrent glioblastoma. It is well documented that both radiotherapy and chemotherapy render tumor cells apoptotic and apoptosis is the major mechanism of cell death in the treatment of cancers. However, clinical trials have produced no clear direction about which chemotherapeutic agents, or approaches, could improve survival rates in the treatment of glioblastomas.

Cellular apoptosis is viewed as an active process that is initiated by the cell’s recognition of a non-correctable cellular abnormality which then proceeds to a state of non-necrotic cell death. Integrins are proteins on the surface of the cell that interact with the surrounding cell matrix whereby they promote an organized cytoskeleton and transduce survival signals. By the use of real time RT-PCR my experiments will determine the transcription rate of the cells integrins as the cells proceed through apoptosis. By the use of flow cytometry experiments, the types of alpha and beta integrins on the surface of the LN-18 cells will also be determined.

The current outlook of most laboratories is that metalloproteinases secreted from tumor cells enhance invasiveness by degrading the tumor cells’ extra-cellular matrix. Currently the scientific community is paying little attention to what is heretofore unrecognized and is being presented here—that the apoptotic enhanced secretions of metalloproteinases have the ability to feedback on the tumor cells along with enhancing the degradation of the extra-cellular matrix, and thereby enhance the invasiveness of those cells in the tumor mass that are chemotherapeutic resistant.

Throughout this coming summer, I will be performing experiments to determine if there is a relationship between integrin degradation and invasiveness. I will also be testing the hypothesis that apoptotic cells assist the invasiveness of non-apoptotic tumor cells.

There is a national movement to incorporate undergraduate research in the student’s experience. There is a strong belief that an undergraduate research experience enhances the overall quality of an institution in meeting the institutional strategic plan. In particular, as the strategic plan relates to quality education and student success. This research specifically supports FSU’s strategic plan in many ways. The perspectives gained through performing undergraduate research under the close guidance of an experienced faculty mentor will enhance my performance in classroom work. It sets examples for other majors by highlighting the
advantages of conducting research in a sustained and close relationship with a faculty mentor. It helps confirm my commitment to obtain a terminal degree. The presentation of results to a scientific audience will increase integration of global awareness across the college experience. The findings of this research will aid in the identification of new programs to meet the needs of ongoing local, regional, and national cancer research programs. This project will provide several students, prior to graduation, the opportunity to participate in research experiences.