Hannah Poulette
UVM Undergraduate Research 2014
Abstract

The development of ovarian cancer requires upkeep of a complex microenvironment that supports tumor growth by reducing immune response, degrading the surrounding supportive tissue, and promoting angiogenesis (new endothelial blood vessel growth). The goal of this project is to understand the role of the protein synthesis regulator, threonyl-tRNA synthetase (TARS), in angiogenic signaling. Prior research has shown that TARS promotes angiogenesis via the stimulation of migrating endothelial cells. To understand the mechanisms underlying the angiogenic influence of TARS, cultured human umbilical vein endothelial cells (HUVECs) were used to examine extracellular interactions and how they affect growth, migration and stress signaling pathways. Western blot was used to quantify the phospho-proteins activated by TARS through downstream signaling pathways including P-ERK, P-AKT, and P-NFkB. The TARS inhibitor, BC194, was also used to confirm that results are TARS-specific. Although positive controls indicated activity of P-ERK and P-NFkB, TARS did not elicit a significant response under the conditions tested thus far. It is possible that the culture conditions prevented the response, thus more experiments are planned to expand on these results. This research will provide important information to the multifaceted project that seeks to understand angiogenesis in the development of ovarian cancer. Future experiments will include membrane-interaction assays and cell imaging to identify the TARS receptor and the control of TARS secretion, as well as the direct effects of TARS on endothelial cell migration. Overall, the results of this research will contribute broadly to the field of biology by analyzing a previously unknown connection between TARS, the tumor microenvironment, and the angiogenic response. This project will also have clinical and public health impact, as it will contribute to validating the potential for TARS as a diagnostic marker or target for treatment of ovarian cancer.