

The Interaction between ERK1, ERK2 and ERK 5 in Expression of Genes that Regulate Malignant Mesothelioma Tumorigenesis: Is it a Team Effort?

Malignant mesothelioma (MM) is a rare and aggressive cancer that arises from the mesothelial layer lining the peritoneal and pleural cavities. Of interest to this study is the pleural form of mesothelioma, which is primarily caused by inhalation of asbestos fibers. The role of the extracellular signal-regulated kinase (ERK) family in promoting cell injury, cell repair as well differentiation and carcinogenesis is well established. Furthermore, in our previous work utilizing microarray analysis, we have been able to identify the altered expression in human MM cells of multiple genes that are regulated by ERK1, ERK2, and ERK5, respectively, that may contribute to the malignant characteristics of MM. The objective of this study is to identify the similar and unique genes that are regulated via ERK1, ERK2 and ERK5 and support development and progression of MM. For this purpose we will be utilizing novel data analysis tools such as Partek® in conjunction with exploratory multivariate analysis and linear modeling. Additionally, we will utilize Ingenuity Pathway Analysis® to elucidate the molecular mechanisms of the ERK family regulated genes that promote the progression of MM. This unique analysis will allow us to understand how these three signaling molecules regulate the expression of similar and/or unique sets of genes in MM cells and the corresponding biological pathways that trigger the development and progression of MM, thus allowing us to design gene-specific strategies to control the aggressive cancer. This Project is supported by the Department of Pathology Masters Program at The University of Vermont, Mesothelioma Applied Research Foundation, VCC/LCCRO and NCI PO1CA114047.