THE ROLE OF TOLUENE, 2-BUTANONE, AND ACETONE IN REGULATING MYOSIN REGULATORY CHAIN (MRCL3) AND CYTOKINE EXPRESSION IN PANCREATIC CANCER

Jameka N. Grigsby and Kenneth Ndebele

Laboratory of Cancer Immunology Target Identification and Validation, College of Science, Engineering and Technology, Jackson State University, Jackson, Mississippi, USA

Abstract: Pancreatic cancer is the most lethal of all cancers. Patients diagnosed with this disease die within six months 95% of the time. There is one currently known conventional chemotherapy for pancreatic cancer and it provides minimal and disappointing benefits. Our strategic efforts are to identify and validate potential molecular therapeutic targets against pancreatic cancer and how they are regulated. Toluene, 2-Butanone, and Acetone pose an environmental health hazard to humans and yet there are very limited carcinogenic data and effects reported. We hypothesize that toluene, 2-butane, and acetone influence immunological microenvironment of pancreatic carcinoma by modulating cell survival, death and tumor growth through Myosin Regulatory Chain (MRCL3). MRCL3 is a regulatory protein which has been implicated in cytokinesis, receptor capping, and cell locomotion. Our studies have demonstrated that silencing MRCL3 significantly inhibited the proliferation and increased cell death of BxPC3 cells compared to the controls. The regulatory effects of acetone, 2-butane, and toluene on MRCL3 were also examined in BxPC3 cells. We have shown that toluene and 2-butane significantly increased BxPC3 cell proliferation while acetone showed no effect compared to the controls. However, we also observed a greater inhibition of cell proliferation upon silencing MRCL3 in BxPC3 cells and treatment with acetone, 2-butane, and toluene. These results imply that toluene and 2-butane exhibit carcinogenic effects in the pancreas. Given the lack of promising pancreatic cancer drugs and data reported on 2-Butanone and Toluene carcinogenic effects, this study sheds insights on possible carcinogenic effects of these environmental solvents in the pancreas.

Keywords: Myosin regulatory light chain, pancreatic cancer, 2-Butanone