Bioanalytical method development for the detection of Rac/Cdc42 inhibitor MBQ-167 in mouse tissue

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Metastatic breast cancer is the second most common cancer in women, in the United States. The mortality rate of breast cancer has decreased approximately 40% in the last 25 years due to advancement in treatment and diagnostics. However, it is estimated that 20-30% of all breast cancer patients will develop metastatic breast cancer (1,2). Therefore, we are developing targeted therapeutics to reduce cancer cell migration and metastasis. The novel small molecule MBQ-167 inhibits Rac and Cdc-42, which are proteins involved in cancer cell migration and invasion (2). *In vivo* studies have shown that MBQ-167 inhibits mammary tumor growth and metastasis in immunocompromised mice by ~90% (3). However, to continue validating this drug for FDA approval, it is necessary to study the pharmacokinetic profile of the drug, which would elucidate the absoprtion, tissue distribution, metabolism, and excretion of the compound in the body (3). Hence, it is necessary to develop a rapid and sensitive method to quantify MBQ-167 in tissues. Selective and sensitive analytical methods for the quantitative evaluation of drugs and their metabolites are critical for the successful conduct of preclinical studies. Our preliminary data suggests that supercritical fluid chromatography coupled with electrospray ionization tandem mass spectrometry (SFC-MS/MS) is a method that can rapidly detect MBQ-167 in mouse plasma with high accuracy, precision, and selectivity. However, further studies are needed to determine if this method can be successfully applied to the detection of MBQ-167 in tissue. The purpose of this study is develop a method for the quantification of MBQ-167 in mouse tissue using SFC/MS/MS. This study is supported by RISE (NIH/NIGMS 5R25GM01151-16).