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Carrie Stump
Washington University in St. Louis

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Analysis of Nicotine Metabolism by Flavin-Containing Monooxygenase and Cytochrome P450 Enzyme Activity in Male and Female C57 Black Mouse Tissues at Different Stages of Development

Carrie Stump

Mentor: A. Joseph Bloom

Nicotine addiction is a major health concern for human populations. Many people smoke; however, people also have difficulty quitting smoking. As a result, it is important that we begin to develop an understanding of the biochemical basis of nicotine addiction. Mice are often used as a good experimental model for nicotine dependence. Flavin-Containing-Monooxygenase protein (FMO) three is known to contribute to nicotine dependence and its expression is known to influence nicotine addiction behavior in humans. This study focuses on the activities of FMOs one and three in male and female C57 Black mouse tissues. As one goal of research in the Bloom Lab is to develop a mouse model for nicotine addiction and withdrawal, understanding how FMO activity varies in different mouse tissues at different stages of mouse development (mouse ages) is critical. Based on prior mRNA studies in 129/SV mice performed by Janmohamed et al., it was hypothesized that FMO one should show activity in all tissues at some level in all stages of mouse development while FMO three should show greatest activity after three weeks of mouse development. Microsomes of mouse brain, liver, lung, and kidney tissues were prepared and then incubated with nicotine in order to elucidate the amount of metabolite from FMO one and three formed. Metabolites were analyzed and quantified by High Performance Liquid Chromatography Mass Spectrometry (HPLC-MS). Results are expected to demonstrate that the activity of FMO one and three matched patterns predicted by the hypothesis.