**PROJECT TITLE:** Evaluating buprenorphine metabolism in opiate-addicted mothers and fetal tissue as a predictor of neonatal abstinence syndrome in rural Appalachia.

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The number of opioid abusing pregnant women is alarmingly high. A recent study in West Virginia showed that in a one month period 7.2% (55/759 births) of umbilical cord specimens were positive for some form of opioid (Stitely, Calhoun et al. 2010). This has obvious impact on the neonates and results in an increase in the likelihood of neonatal abstinence syndrome (NAS) with estimates ranging from 50-80% of neonates undergoing NAS in untreated populations (Chiriboga 1993, Coyle, Ferguson et al. 2002). At Marshall, Dr. David G Chaffin of the department of OB/GYN has recently launched a Maternal Addiction and Recovery Center (MARC) program, which uses buprenorphine as medication-assisted treatment in pregnant opioid abusing women. Though this program has led to a significant drop in the incidence of NAS for the buprenorphine group it has not been possible to date to predict which of the babies are most likely to undergo NAS. The role of this proposal is to investigate potential predictors for NAS in the buprenorphine program. Our overall hypothesis is that the incidence of NAS is due to a change in pharmacokinetic and/or metabolic profiles due to alterations in Phase I-III metabolism of buprenorphine in either the mother or fetus, or potentially both, that leads to increased exposure of the fetus to pharmacologically active buprenorphine metabolites. The objectives of this study are to investigate the role of differential buprenorphine metabolism in NAS, and determine the correlation with NAS scores. This project will add additional cord and cord tissue samples to our ongoing pilot project which has currently collected 30/40 samples (75%). Funding of this submission will allow for an additional collection of 40 samples along with expansion to measure buprenorphine and metabolites in maternal blood and placenta. Funding will also enable us to initially investigate expression and activity profiles (i.e. SNPs) of major phase I enzymes for buprenorphine metabolism. This submission is not a duplication or overlap in funds with the currently funded pilot project. To carry this out we have 3 specific aims:

SPECIFIC AIM 1: Determine the expression profiles of opiate drugs and their metabolites in maternal blood, cord blood, cord tissue, and placenta.

SPECIFIC AIM 2: Determine expression profiles of regulators of maternal, placental and neonate phase I metabolism.

SPECIFIC AIM 3: Analyze maternal and neonate patient records and correlate neonate outcomes to buprenorphine metabolism profile.