

Submitter: Miguel Angel Brieño-Enríquez  
Submitted email: [brienoenriquezma@upmc.edu](mailto:brienoenriquezma@upmc.edu)  
PI: Miguel Angel Brieño-Enríquez  
PI email: brienoenriquezma@upmc.edu

## **Reproductive decline and epigenetic effects of in utero opioid exposure**

Timothy Robinette<sup>1</sup>, Meagan Goben<sup>1</sup>, Miguel Angel Brieño-Enríquez<sup>1,2</sup>

<sup>1</sup>Magee-Womens Research Institute, Department of Obstetrics, Gynecology & Reproductive Sciences, University of Pittsburgh; <sup>2</sup>Aging Institute, University of Pittsburgh School of Medicine

Opioid use has quadrupled over the past decade, with 259 million prescriptions in the United States. Every 3 minutes, a woman seeks care in an emergency department related to prescription opioid misuse, and more than 660 women died from opioid overdose in 2010. A Medicaid database cohort study of 1.1 million pregnant women revealed a 23% increase in opioids prescribed from 2000 to 2007, and according to the National Survey on Drug Use and Health (NSDUH) (2005-2014), 5.1% of pregnant women reported nonmedical use of prescription opioids. The increasing prevalence of opioid use in pregnancy has led to a concomitant fivefold increase in neonatal abstinence syndrome (NAS). Early human development during pregnancy and infancy plays a key role in the risk of chronic diseases and, possibly, of addiction. Individuals with a family history of drug abuse have an eightfold increase in the likelihood of drug use, suggesting familial transmission of substance abuse disorders. Evidence suggesting the inheritance of epigenetically mediated phenotypes, multigenerationally and transgenerationally, in mammals is growing rapidly. In fact, several animal studies have reported that there is an altered response to morphine, causing psychological and structural changes in the brains of offspring of exposed parents. In this study we evaluate how the exposure to opioids *in utero*, disrupts the specification, and epigenome of primordial germ cells (PGCs), the embryonic precursors of both egg and sperm. These changes will affect reproductive capabilities but will also be able to carry defects in epigenetic markers from one generation to another.