Transgenerational epigenetic inheritance associated with prescription opioids abuse:
Like mother, like child?

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Recent statistics from the Centers for Disease Control and Prevention (CDC) show that every
day, more than 115 Americans die from overdosing on opioids. Adding another layer of
complexity is the increased risk of dependency on prescription opioids such as oxycodone (oxy)
during pregnancy and postpartum. Limited studies have linked maladaptive behaviors and
cognitive deficits in exposed offspring, and a significant knowledge gap remains in
understanding how short- and long-term oxy exposure impacts inherent behaviors in the
exposed offspring and whether these changes persist in the subsequent generations. We
accordingly have developed an animal model using Sprague Dawley rats to mimic oxy exposure
in utero and post-natally to examine long-term consequences of its abuse on the exposed
offspring (F1) as well as subsequent unexposed generations (F2). Using RNA-Seq on RNA
isolated from the nucleus accumbens (NAc), a region of the brain involved in reward and
sensitive to drug abuse, we identified key changes in genes associated with synaptic signaling
and neuron differentiation in both the F1 and F2 generations of each group. To further elucidate
how changes in the epigenetic milieu impact glutamatergic and dopaminergic systems, we
conducted behavioral tests to assess repetitive behaviors and social alterations among the
experimental groups and between the two generations. Sex differences were also considered
during the behavior tasks. Given the increased use of opiates (both medical and non-medical),
understanding the persistent developmental effects of these drugs will delineate potential risks
associated with opiate use beyond the direct effects on the user.