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Transgenerational transcriptomic changes associated with prescription opioids abuse: How far has the apple fallen from the tree?

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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, including heroin and prescription opioid pain relievers. Emerging evidence clearly indicates an increased risk of dependency on prescription opioids such as oxycodone (oxy) during pregnancy and postpartum. While limited studies have linked maladaptive behaviors and cognitive deficits in exposed offspring, a significant knowledge gap that remains is understanding how short- and long-term oxy exposure impacts the transcriptomic architecture in the exposed offspring and if these changes persist in the subsequent generations. We accordingly have developed an animal model mimicking oxy exposure *in utero* and *post-natally* to examine long-term consequences of its abuse in the exposed offspring (F1) as well as subsequent generations (F2) in the absence of drug exposure. Using RNA-Seq on nucleus accumbens (NAc), a region of the brain involved in drug reward, we identified key changes in genes associated with chromatin modifications, opioid addiction, synaptic plasticity, neurotransmission, and more. Notably, key phenotypic differences, such as alterations in head size, body weight, and body length, were also observed. Based on these initial findings, we are now examining changes in the glutamatergic and dopaminergic systems, including behavioral alterations between the two generations. 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.