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## **PLX-PAD placental derived mesenchymal like adherent stromal cells as an effective cell therapy for cocaine addiction in a rat model**

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**Aims:** Mesenchymal stem cells (MSCs) research is on the verge of a breakthrough for neurodegenerative disorders treatment and were proven to navigate within the brain to specific pathological regions. We examined the longitudinal effect of placenta derived mesenchymal like cells (PLX-PAD) in a rat model for addiction. We combined the intranasal administration (IN) method that enables a new mode for non-invasive and safe administration with MSCs as a novel treatment of addiction.

**Methods:** Rats were trained to self-administer cocaine or saline daily until stable maintenance levels were attained. Before an extinction phase, viable PLX-PAD cells were administrated IN followed by BrdU i.p. and rats were monitored behaviorally for craving. At the conclusion of the experiments brains were stained for BrdU & Neun (a marker for adult neurons).

**Results:** We found that PLX-PAD significantly lowered cocaine seeking behavior by decreasing active lever presses in the relapse test. In addition, PLX-PAD cells were found to navigate and home to addiction related sites in the brain such as the Nucleus Accumbens and Dentate Gyrus. Moreover, cocaine self-administration attenuated neurogenesis in the hippocampus and PLX-PAD normalized it parallel to alterations in BDNF and specific miRNAs expression.

**Conclusion:** PLX-PAD attenuates cocaine seeking behavior probably through their capacity to migrate to specific mesolimbic regions, improving their plasticity by restoration of neurons in the hippocampus. We postulate that IN cell therapy is a safe and effective approach for addiction and may offer an efficient rehabilitation rather than a mimetic effect as other available clinically-used pharmacological agents do.