

## Commentary on - Human Embryonic Retinal Pigment Epithelial (Rpe) Cell Transplants for Chronic Refractory Cocaine Addiction

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Chronic refractory drug addiction remains a major cause of morbidity, mortality, and growing related healthcare expense in the United States. Therefore, a novel method of treatment for such severe refractory patients is required. Animal models of cocaine addiction using laboratory rats that self-administer the drug have a proven history of translational relevance. In the experiments describe in the recent publication, Venkiteswaran et al., we describe experiments where we examined cocaine seeking in rats following bilateral transplantation of human embryonic retinal pigment epithelial cells (hRPECs) or placebo into the nucleus accumbens (NAc) [1]. Human embryonic retinal pigment epithelial cells secrete the dopamine precursor, L-Dopa would be good to tell the reader what all they do here. The results showed that the out bred Sprague-Dawley male rats naturally segregated into two groups: one that self-administered a high amount of cocaine intravenously (IV) and a second group that self-administered a low amount of cocaine [2]. This finding is consistent with our previously published findings with cocaine and heroin and appears to reflect the individual differences seen in humans who abuse cocaine [3-5].

Although the cause of these individual differences is not known, results also showed that rats with a history of high drug taking that received human embryonic RPE cell transplants bilaterally into the NAc exhibited significantly less cocaine seeking following a period of abstinence than did high drug-taker vehicle transplanted controls. Histological examination of the brains showed excellent graft survival in all groups of rats and an increased survival of TH positive neurons in the ventral tegmental area (VTA) in RPEC transplanted rats compared to the vehicle-transplanted controls. This finding suggests that dopaminergic VTA neurons are vulnerable to cell death following just 2 weeks daily self-administration of cocaine. Importantly, these neurons appeared to be partially rescued when transplanted with the hRPECs in their axonal fields within the NAc. One potential mechanism through which this novel therapy could be working is via the local replenishment of dopamine in the NAc on a continuous basis and by

production of growth factors, which are retrogradely transported to VTA to prevent neurodegeneration [6,7]. Further studies are underway to elucidate these mechanisms and to further develop this as a potential therapeutic strategy for chronic drug addiction. One major advantage of this form of therapy using RPECs is that they do not require chronic immunosuppression, do not require permanent installation of any hardware, and can be used in 1000s of patients from a single donor since the cells can be cultured and expanded without any risk of tumor formation [8].

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Received March 29, 2016; Accepted April 19, 2016; Published April 26, 2016

**Citation:** Venkiteswaran K, Subramanian T, Sue-Grigson P (2016) Commentary on - Human Embryonic Retinal Pigment Epithelial (Rpe) Cell Transplants for Chronic Refractory Cocaine Addiction. *Health Care: Current Reviews* 4: 165. doi: [10.4172/2375-4273.1000165](https://doi.org/10.4172/2375-4273.1000165)

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