Submitter Name: Prasun K. Datta
Submitted email: dattapk@temple.edu

Modulation of glutamate transporter, EAAT2 expression by epigenome editing.

Prasun K. Datta[1], Masoud Shekarabi[1] and Satish Deshmane[1]

[1]Department of Neuroscience, Lewis Katz School of Medicine at Temple University

Solute carrier family 1, member 2 (SLC1A2) encodes the glutamate transporter 2 (EAAT2) protein primarily expressed in astrocytes and is responsible for the majority of glutamate uptake in brain areas implicated in NeuroHIV and addiction. In the current study, we investigated whether epigenome based editing can be harnessed to activate HIV-1 Tat and cocaine mediated dysregulation of EAAT2 expression in astrocytes. Using multiple approaches, we show that the SLC1A2 promoter is induced by the gRNAs in the presence of dCas9 fused to p300 catalytic domain in primary astrocytes and cell lines. Induction of SLC1A2 promoter led to increase in EAAT2 mRNA and protein expression. In addition, we show that the co-transfection of gRNAs with dCas9-p300 can mitigate HIV-1 Tat and cocaine induced downregulation of EAAT2 RNA in astrocytes. Collectively, these results demonstrate that epigenome editing system can be used for potential induction of EAAT2 expression not only in NeuroHIV but also for ALS and Alzheimer's disease and addiction.