Submitter Name: Suhas Ganesh
Submitted email: suhas.ganesh@yale.edu
PI Name: Deepak Cyril D'Souza
PI email: deepak.dsouza@yale.edu

Molecular intersections of cannabis exposure and psychosis expression using patient derived HiPSC neurons

Suhas Ganesh[1], Jose Cortes-Briones[1], Biju Viswanath[2], Odity Mukherjee[3], Daya Ram[4], Pratima Murthy[2], Sanjeev Jain[2], Deepak Cyril D'Souza[1]

[1]Department of Psychiatry, Yale University; [2]Department of Psychiatry, National Institute of Mental Health and Neuro Sciences; [3]Centre for Brain development and repair, Institute for Stem Cell Biology and Regenerative Medicine; [4]Department of Psychiatry, Central Institute of Psychiatry

Background: Cannabis use is a well-recognized risk factor schizophrenia. Epidemiological studies attribute a causal role for cannabis exposure on psychosis outcomes, while GWA studies suggest bidirectional causal relationship. A minority of individuals exposed to cannabis develop psychosis – possibly due to their genetic vulnerability. Putative molecular mechanisms underlying the interaction between the genetic risk and cannabinoids are not understood. The advent of human induced pluripotent stem cell (HiPSC) technology offers a novel opportunity to examine such mechanisms. HiPSC derived neurons from persons with Cannabis Induced Acute and Persistent Psychosis (CIAPP) can facilitate recapitulating cannabinoid exposure *in vitro* and understand convergent etio-pathogenic pathways at cellular level. **Significance:** The changing landscape of cannabis use in the US, specifically among the young, calls for studies aimed at understanding its potential negative consequences. **Hypothesis:** With exposure to THC, transcriptomic profile of HiPSC derived neurons from CIAPP will show greater overlap with schizophrenia relative to controls. **Aim:** To compare transcriptomic profile in HiPSC neurons at baseline, and following THC exposure, between age and gender-matched individuals with psychosis unrelated to cannabis, and healthy controls. **Preliminary results and discussion:** In an ongoing NIDA funded study, (R21DA041539: D'Souza), we have characterized the phenotype of CIAPP. Preliminary results suggest partial overlap between CIAPP and schizophrenia at baseline (PANSS domain scores, EEG measures of connectivity) but rapid recovery with inpatient treatment. We propose to generate HiPSC neurons from ten cases of CIAPP and compare the cellular phenotype including transcriptomic profile with schizophrenia and healthy control lines upon exposure to cannabinoids.