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Deciphering synaptic perturbations associated with HIV and Methamphetamine mediated CNS dysfunction

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Drugs of abuse represent a significant co-factor in HIV infection and their synergy can lead to accelerated disorders. With the advent of combined antiretroviral therapy (cART), most severe cognitive impairments are now supplanted by milder, less profound cognitive deficits that can have significant negative ramifications on individuals' activities of daily living. Our research focuses on methamphetamine (METH), a potent psychostimulant and our working hypothesis is that the synaptic molecular composition is altered in HIV infected individuals who use METH. Applying a productive rationale strategy leading to the identification of mechanisms that reflect cellular responses to HIV/drug abuse, our previous work on quantitative proteomic profiling on synaptosomes from rhesus caudates identified a potential lead- the neuron specific Na^+/K^+ ATPase alpha 3 subunit (ATP1A3), to be up regulated in the SIV+METH treated group compared to the SIV group. Apart from its well-established role as an ion pump in maintaining electrochemical gradient, emerging studies have implicated ATP1A3 as a receptor for the endogenous steroid ouabain and eliciting signal transduction cascades via MAP kinases especially the ERK1/2 pathway. Examining possible parallels with METH that led to phosphorylation of ERK1/2 from our preliminary data, we hypothesize that a novel mechanism of action of METH in the CNS is to interact with ATP1A3 and elicit signaling. Given the considerable evidence of potential ERK activation with cell survival, proliferation and survival, our current work focuses on defining the impact of HIV and METH on ATP1A3 in modulating this biological pathway as well as assessing the functional studies and evaluating the biological consequences in the brain.

Biography

Dr. Gurudutt Pendyala completed his Ph.D in 2005 from University of Fribourg, Switzerland and postdoctoral training from The Scripps Research Institute. He is currently a Faculty at the University of Nebraska Medical Center since 2009 and serves as a reviewer for 3 peer-reviewed journals including "omics"-The journal of integrative Biology.