

## HIV-1 infection and Cocaine Go hand in HAND

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Intravenous drug use (IVDU) and HIV infections are two linked global health crises since needle sharing is a well-recognized mode of HIV transmission. Cocaine, often abused by HIV-infected patients, has been suggested to worsen HIV-associated neurocognitive disorders (HAND) via unknown mechanisms. Our recent research interest has focused on understanding molecular mechanisms by which cocaine accelerates pathogenesis of HAND by impacting the functioning of various CNS cell types. In this area, we have demonstrated that: 1) In macrophages, cocaine enhances virus replication and activation, 2) In microglia cocaine upregulates the expression of key chemokine MCP-1, leading to increased influx of inflammatory cells in the brain; 3) In neurons cocaine potentiates neurotoxicity mediated by HIV-1 envelope protein gp120; 4) In human brain microvascular endothelial cells, cocaine induces the expression of the adhesion molecule ALCAM as well as the cerebrovascular permeant platelet-derived growth factor (PDGF)-B chain, both of which impair blood brain barrier integrity resulting again in augmentation of endothelial permeability as concomitant increased monocyte transmigration; 5) More recently we have also shown that cocaine-mediated targeting of Notch-1 receptor in brain endothelial cells can also result in induction of PDGF-BB. Functional implication of up-regulated PDGF-BB as a vascular permeant was confirmed both in cell culture and *in vivo* model systems using permeability and transmigration assays. In summary, besides its addictive role in the CNS, cocaine also functions as an adjunct agent that has the capacity to negatively impact the functioning of almost all the cells of the CNS leading to increased neuroinflammation and thus contributing to the pathogenesis of HAND.

### Biography

Shilpa Buch completed her Ph.D at the age of 25 years from M.S. University in Baroda, India and postdoctoral studies from University of Western Ontario, London, Canada. She is a Professor and Vice Chair for Research at University of Nebraska Medical Centre. She has published more than 85 papers in reputed journals, has served on NIH study sections and is an editorial board member of repute.