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Contribution of Methamphetamine-Induced Dysregulation of RNA Methylation to Promoting HIV Infection in Microglia/Macrophages

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The global rate of HIV infection and number of AIDS-related deaths have dramatically declined due to the expanding access to combinatorial anti-retroviral therapy (cART). However, the HIV epidemic remains and there is still no cure for HIV infection, as cART does not eradicate HIV. The central nervous system (CNS) is a key anatomical “sanctuary site” for HIV infection. Microglia are the foremost cells infected by HIV in the CNS that form a major and stable viral reservoir and release neurotoxic factors that promote neuroinflammation and contribute to HIV-associated neurocognitive disorders (HAND). Methamphetamine (METH), a potent addictive psychostimulant, is one of the most abused drugs in the United States. METH abuse is highly prevalent in HIV-infected individuals and there is the overlap impact of METH use and HIV on the neuronal damage. It becomes urgent to understand the role of interplays between METH and HIV in the pathogenesis of HAND. We and other have shown that METH promotes HIV replication and induces neuronal inflammation, which likely impacts the dynamics of HIV infection in the CNS. However, the underlining mechanisms are still not fully understood. We’ve initiated the efforts to investigate the impact of METH on m5C RNA methylation, one of the most abundant modifications of both HIV and host mRNAs. We recently conducted RNA-seq and RNA-bisulfite-seq studies for METH-treated primary macrophages. Our data indicated that METH dysregulates the NSUN1/2 expression as well as the m5C RNA methylation of host factors in macrophages/microglia, which would facilitate HIV infection in the CNS.