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Role of Microbiota-derived Butyrate in Depression Associated with HIV-1 and Opioid Use

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Major Depression is prevalent in HIV-patients using opioids. Depression in HIV-patients is associated with poor adherence to antiretroviral therapy and higher mortality rates. Growing evidence suggests a strong link between HIV-associated depression and gut microbial dysbiosis. In addition, we have reported that opioid use exacerbates HIV-induced gut dysbiosis and mucosal barrier damage, which results in translocation of the microbes to circulation and systemic inflammation. Thus, therapeutic strategies aimed at restoring gut homeostasis may alleviate depression associated with HIV-1 and opioid use. Here, we investigated the role of short-chain fatty acid Butyrate in depression associated with HIV-1 and opioid use. Butyrate is naturally derived from microbial fermentation in the gut and is a known inhibitor of histone deacetylases. Interestingly, depressed individuals and HIV-patients show a lower abundance of butyrate-producing bacteria. In addition, butyrate supplementation reduces the side effects of opioid use, including peripheral hypersensitivity, neuronal hyperexcitability and antinociceptive tolerance. Taken together, we hypothesized that “opioid use and HIV-1 through depletion of butyrate-producing gut bacteria and reduction of butyrate levels contributes to neuroinflammation and depression”. We observed that spontaneous morphine withdrawal induces depression-like behavior more severely in HIV-1 transgenic (Tg26) mice, compared to wild-type mice, in the tail-suspension test. In addition, morphine treatment significantly reduced fecal butyrate levels in mice. Ongoing experiments will determine whether butyrate-supplementation will alleviate opioid withdrawal-induced depression-like behaviors in Tg26 mice. In summary, the outcome of this study will help in providing therapeutic development for both prevention and acute treatment of HIV-patients susceptible to depression in the future.