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Human immunodeficiency virus type i neuropathogenesis in the age of combined antiretroviral therapy: The role of inflammation

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ore than 30 years into the HIV epidemic, significant worldwide morbidity and mortality due to infection with this Mvirus continues despite the increased availability of combination anti-HIV therapies, which can effectively suppress viral replication. HIV enters the central nervous system early after penetrating mucosal portals and disseminating where it infects and replicates robustly in resident microglia and macrophages. Neurons do not serve as hosts for HIV and the injury and dysfunction seen in individuals with HIV-associated cognitive impairment occurs through a network of indirect toxic mechanisms, many of which remain to be defined. Cellular activation of multiple cell types in the brain, as a result of HIV infection, leads to levels of inflammation that are in excess of that seen under normal homeostatic conditions. We have been investigating the role of the proinflammatory cytokine osteopontin in the pathogenesis of HIV-associated neurocognitive disorders (HAND). Osteopontin is an early immune activation marker implicated in the regulation of T-lymphocyte function and balance between cell- and humoral immunity. In macrophages, OPN can regulate cell migration and survival and is elevated in individuals with HAND. We have used a combination of molecular and cellular approaches including next generation high-throughput sequencing (RNA-Seq), surrogate culture models to define the domains of OPN required for its ability to enhance HIV replication, and ex vivo studies using biological samples from HIV-infected individuals with or without cognitive impairment and controls to delineate its role in HIV-related neuropathogenesis. By understanding how HIV commanders macrophage signaling networks, we may be able to develop novel therapeutic strategies to counteract the pathogenic effects of the virus.

Biography

Brown completed her Ph.D from the Albert Einstein College of Medicine of Yeshiva, University and postdoctoral studies at the Aaron Diamond AIDS Research Center. She is the Director of the Johns Hopkins Internship in Brain Science Program, Co-Director of the Developmental Core for The NIMH Center for Novel Therapeutics for HIV-Associated Cognitive Disorders, Co-Director of Translational Research in NeuroAIDS and Mental Health and a Fellow of Keystone Symposia on Molecular and Cellular Biology 2014. Dr. Brown has published 17 papers in reputed journals and serves as Managing Editor for the Frontiers in Bioscience Special Issue Series.

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