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Monocyte/macrophage cathepsin B interactome in HIV-1 neurocognitive disorders

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Chronic human immunodeficiency virus type one (HIV-1) infection leads to a spectrum of neurological and cognitive dabnormalities, known collectively as HIV-associated neurocognitive disorders (HAND). HAND remains prevalent, particularly in its milder forms, despite effective combination antiretroviral therapy (cART). The pathogenesis of HAND is thought to involve HIV-infected perivascular macrophages and microglia, whose activation leads to the release of pro-inflammatory cytokines and other soluble factors toxic to neurons. One factor that may be involved in macrophage-mediated HIV neurotoxicity is cathepsin B, a member of the cysteine protease family. We recently demonstrated that monocyte-derived macrophages (MDM) secreted, cathepsin B has increased neurotoxic activity *in vitro*. In studies of our Hispanic women cohort, we observed increased expression of both cathepsin B and cystatin B in monocytes of women with HAD on cART with no comorbid conditions. Cathepsin B is also upregulated in the CNS of patients with HAND. We hypothesized that cathepsin B is interacting with other proteins that contribute to neurotoxicity. Using immunoprecipitation of cathepsin B in macrophage supernatants and mass spectrometry, we demonstrate that cathepsin B interacts with MMP-9 in uninfected cells but this interaction disappears in HIV infection and develops a new interaction with serum amyloid P component (SAPC). SAPC is related to amyloid deposition in Alzheimer's disease (AD). These results suggest that cathepsin B might be involved in amyloid-beta-related inflammatory response, which results in neuronal death. These studies will significantly advance the HIV field by providing new clinical diagnostic tools, new pathways, and possible complementary therapies against HAND.

Biography

Loyda M Meléndez has completed his PhD and postdoctoral studies from Emory University School of Medicine School of Medicine. She is Professor and director of the Translational Proteomics Center, at the University of Puerto Rico School of Medicine. She has published more than 50 papers in reputed journals and has been serving as an editorial board member. Her diverse preparation in Medical Technology and Experimental Pathology-Immunology provided her the tools to apply knowledge to uncovering mechanisms of pathogenesis against HIV. Her work is reflected in studies of HIV-infected macrophages and the proteins associated with neuropathogenesis.

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