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Proteomics studies of Monocyte / Macrophages in HIV associated neurological disorders

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Macrophages are important reservoirs during progressive HIV-1 infection and in the development of cognitive, behavioral, or motor dysfunction. Mononuclear phagocytes (MP; perivascular macrophages and microglia) are the primary cells infected with HIV-1 in the brain. Thus, investigating differences in protein production, secretion, and signaling of MP is of primary importance to understand the incidence of HIV-1 associated neurological disorders (HAND). The molecular and cellular mechanisms for neuronal impairment evolve from neurotoxic secretory products produced from MP. Although the intracellular mechanisms that affect toxic MP secretions are incompletely known, the efector cell responses do play a pivotal role in CI. Our long-term goal is to provide a better understanding of the intracellular mechanisms that regulate macrophage secretory factors in homeostatic control during progressive HIV infection of the brain and to uncover novel targets for diagnosis and potential therapies. Among many secretory factors, cystatins and cathepsins secreted by MP play broad yet important roles in neuroregulatory responses. In particular, our laboratory and ex vivo experiments have shown differences in cathepsins, cystatins, and superoxide dysmuthase (SOD) in virus-infected monocytes, macrophage culture fluids, and cerebrospinal fluid (CSF) of HIV-seropositive women with CI by proteomic analyses. We have demonstrated increased secretion and activity of these enzymes in response to HIV infection of monocyte / macrophage but not in microglia. The studies with the Hispanic cohort will also clarify the role of cystatins, cathepsins, SOD, and protein identified with quantitative proteomics in HIV-cognitive impairment in the post-HAART era.

Biography

Dr. Meléndez earned her Ph.D. degree in Experimental Pathology & Immunology from Emory University School of Medicine in 1990, where she also completed post-doctoral training. She joined the Department of Microbiology and Medical Zoology of the School of Medicine at the UPR-MSC in 1992. Dr. Meléndez is the Director of the Clinical Proteomics Core at the UPR-MSC. She has published 35 manuscripts, several book chapters, is a co-inventor of 4 patents, and is ad hoc reviewer for NIH and several National and International Journals in HIV, macrophages, Proteomics, and NeuroAIDS.