Disruption of MAM in premature brain aging and HIV-Associated Neurocognitive Disorders (HAND)

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The Mitochondrial-Associated ER Membrane (MAM) is the contact between the membrane fragment of the endoplasmic reticulum (ER) and the outer membrane of the mitochondria. The MAM regulates many neuronal functions including calcium exchange, lipid exchange, intracellular trafficking, and mitochondrial biogenesis. Interestingly, all these processes are affected early during aging, AD, PD, ALS/FTP pathogenesis, and other neurodegenerative conditions. This suggests a role for MAMs in the pathogenesis of these diseases. Patients infected with HIV-1, including those using combinatory Anti-Retroviral Therapy (cART), suffer from impairment of vital organs such as brain, heart, etc. Studies involving HIV-infected patients using cART showed signs of HIV-1 associated neurocognitive disorders (HAND) including spatial memory loss. We and others demonstrated mitochondrial fission and fusion defects in patients with HAND compared to cognitively normal HIV(-) patients. We also have evidence that HIV-1 proteins can cause further mitochondrial dysfunction leading to defects in energy, calcium homeostasis, and synaptic plasticity. All of which are necessary for memory function. Our data gave us the rationale to determine whether viral proteins are disrupting MAM thus causing HAND. We are in the process of testing the integrity of the MAM's physical and functional interactions and exploring changes in mitochondrial fission/fusion and movement all using HIV-1 TAT treated cells. By targeting the MAM dysfunction, we hope to develop new approaches for the treatment of HAND.

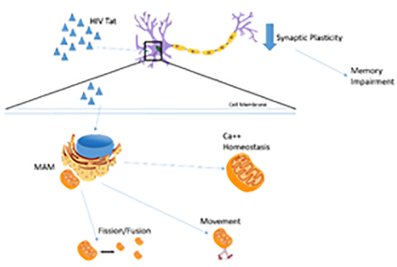

Figure 1: Schematic of hypothesis. HIV Tat protein gets into the neurons and disrupts the normal functioning of the MAM. This causes downstream effects including mitochondrial fission/fusion, mitochondrial movement, and calcium homeostasis impairments. These downstream effects eventually lead to decreased synaptic plasticity and memory loss associated with HIV infection.

Biography

Sterling P Arjona, a third year PhD student at Temple University, he has worked in Bassel E. Sawaya's lab for the past year researching HIV-1's effect on HIV associated neurocognitive disorders (HAND). Prior to joining Temple University, he received his B.S. in neuroscience from Dickinson College. While at Dickinson College Sterling researched Morphology and Histology of Foveolar and Saccular Lungs in Boa Constrictors.

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