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The evolution of the impact of peripheral immune activation on HIV cognitive impairment

Human immunodeficiency virus (HIV) severely impacts the immune system causing phenotypic changes in peripheral cells altering both innate and adaptive immunity. In the acute phase, HIV attacks and kills CD4+T cells, followed by monocyte/macrophage (M/M ϕ) activation and an acute-phase inflammatory response. Approximately 30% of HIV-infected individuals develop an associated dementia caused by toxic soluble factors from activated M/M ϕ . With the introduction of antiretroviral therapy (ART), most infected individuals respond to therapy with a lowering of the viral load to undetectable and reconstitution to normal immune function. However, some individuals do not return to normal immune function and their M/M ϕ continues to be activated. This continued peripheral monocyte immune activation, now chronic, continues to be associated with cognitive impairment as well as other co-morbidities. The factors responsible for this have changed as new biomarkers for milder cognitive impairment are evolving. Since the M/M ϕ migrates to the brain, the activation state of this immune cell is critical. New mechanisms for cell-to-cell communication have been introduced. Exosomes are lipid vesicles normally secreted by a number of cells in the plasma and tissues but are increased and altered in pathological conditions. They can transport functional nucleic acids (mRNAs, miRNAs) and proteins into recipient neural cells. Monocyte-derived exosomes can enter neural cells and contribute to neural cell dysfunction by the transfer of dysregulated miRNAs. Activated monocyte-derived exosomes may contribute to the transfer of neurotoxic cargo from M/M ϕ to resident neural cells. Alternatively, miRNAs within exosomes may be exploited as a therapeutic target to diminish neural cell activation.

Biography

Lynn Pulliam received her PhD from the University of San Francisco Medical School in 1983. She is a Professor of Laboratory Medicine and Medicine at the University of California, San Francisco as well as Chief of Microbiology at the San Francisco Veterans Affairs Medical Center. She is the past President of the International Society for Neurovirology and serves on several editorial boards.

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