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Deregulation of microRNAs by HIV-1 Vpr protein leads neuronal dysfunction

Ruma Mukerjee
Temple University, USA

Abstract

HIV-infected patients develop neurocognitive disorders characterized by neuronal dysfunction. The lack of productive infection of neurons by HIV suggests that viral and cellular proteins, with neurotoxic activities, released from HIV-1-infected target cells can cause this neuronal deregulation. The viral protein R (Vpr), a protein encoded by HIV-1, has been shown to alter the expression of various important cytokines and inflammatory proteins in infected and uninfected cells; however the mechanisms involved remain unclear. Using a human neuronal cell line, we found that Vpr can be taken up by neurons causing: (i) deregulation of calcium homeostasis, (ii) endoplasmic reticulum-calcium release, (iii) activation of the oxidative stress pathway, (iv) mitochondrial dysfunction and synaptic retraction. In search for the cellular factors involved, we performed microRNAs and gene array assays using human neurons (primary cultures or cell line, SH-SY5Y) that we treated with recombinant Vpr proteins. Interestingly, Vpr deregulates the levels of several microRNAs (e.g. miR-34a) and their target genes (e.g. CREB), which could lead to neuronal dysfunctions. Therefore, we conclude that Vpr plays a major role in neuronal dysfunction through deregulating microRNAs and their target genes, a phenomenon that could lead to the development of neurocognitive disorders.

Biography

Dr. Ruma Mukerjee is an Assistant Professor in Fels Institute at Temple University. She received her PhD from KG Medical College, India and completed her postdoctoral training in University of Pennsylvania. Dr. Mukerjee has been involved in biomedical research for several years and published 33 papers in reputed journals. Currently, her research involves studying the role of microRNA in neuronal dysfunction.