BIOINFORMATION
Discovery at the interface of physical and biological sciences

open access www.bioinformation.net Editorial

Volume 8(25)

Molecule of the month: HIV-1 protein Vpr and miRNA

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Received December 11, 2012; Accepted December 11, 2012; Published December 19, 2012

miRNAs are a well-established RNA phenomenon. Previously, we analyzed the involvement of HIV-1 protein Tat in cellular gene networks and aspects of its interaction with miRNAs **[1].** Here we mention an additional HIV-1 protein, HIV-1 viral protein R (Vpr) that interacts with miRNAs and it is involved in gene expression networks. The manipulation of miRNA expression is anticipated to become important in the attack on disease. miRNAs are generally derived from non-coding portions of the human genome and are intricately involved in gene expression control **[2].** Moreover, it is estimated that although 1% of human genes are miRNAs, these miRNAs are involved in the control of gene expression of 10% of all the genes **[3].**

HIV-1 modifies the miRNA profile of infected cells. On the one hand, HIV-1 infection suppresses miRNAs that promote proteins that interfere with HIV-1 replication. Contemporaneously, on the other hand, HIV-1 enhances miRNAs that promote proteins that are beneficial for the replication of HIV-1 **[4].** There are diverse effects on cells and tissues due to HIV-1 infection. For example, HIV-1-infected individuals often undergo pathological brain changes that result in disorders of cognition. Neuronal dysfunction is a hallmark of such pathologies. Proteins released from HIV-1-infected cells are associated with such dysfunction and HIV-1 Vpr is one such protein **[5].** HIV-1 Vpr exhibits complex functions during HIV-1 replication and is involved in viral replication, shuttling between the infected cell's nucleus and cytoplasm **[6].** In neuron culture, *in vitro*, exposure to Vpr results in several adverse changes including v- synaptic retraction, mitochondrial dysfunction, oxidative stress pathway activation, expression of inflammatory molecules including cytokines, calcium homeostasis dysregulation, and calcium release from endoplasmic reticulum. Vpr dysregulates miRNAs including miR-34a as well as the miRNA target genes IRBIT, SERP1, SIRT1, NEFM, Drp-1, Orai, STIM1, IP3R, and CREB **[5].**

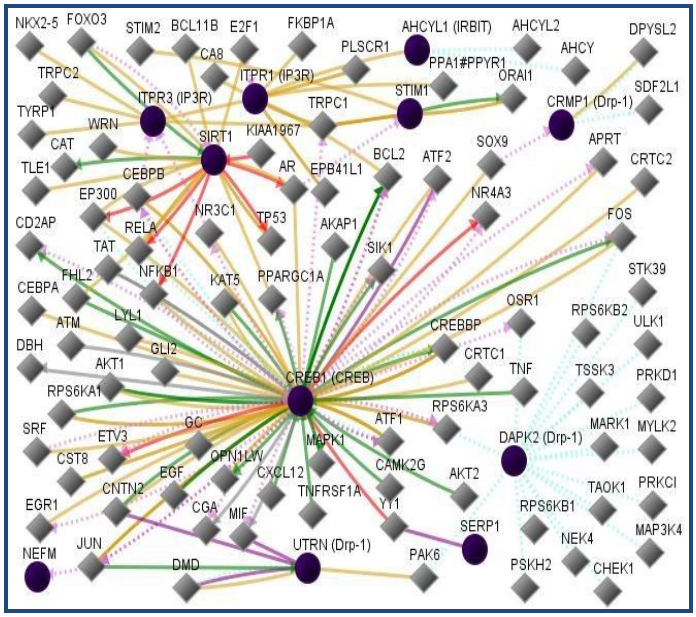

Figure 1: Network of input proteins and the input neighbors of these proteins. Consequent to HIV-1 infection, expression of these proteins may be modulated by miRNAs. In this figure, line-colors and various interactions with other genes are red Down-regulation, green Up-regulation, beige Regulation, purple Co-expression, brown Physical Interaction, turquoise dotted Predicted Protein Interaction, and mauve dotted Predicted TFactor Regulation (GenePro SA Biosciences, http://www.sabiosciences.com/).

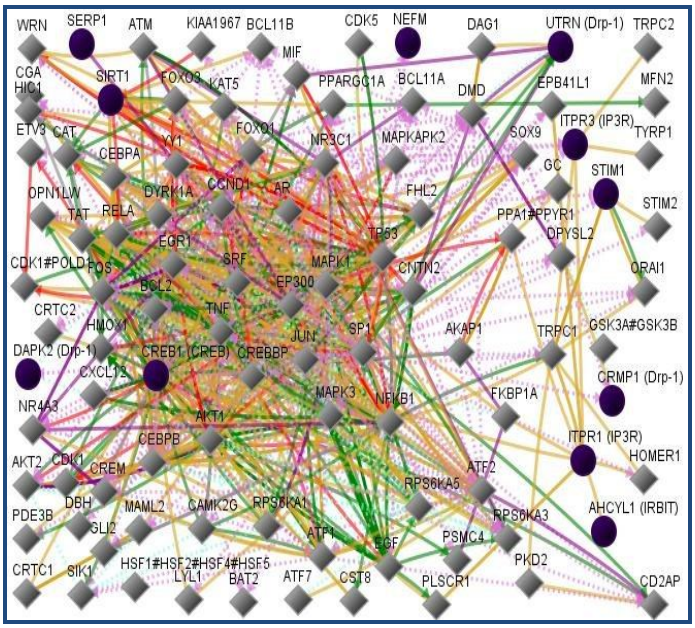

Figure 2: Network of neighbor interactions of the input genes with the various networks through which they interact. Consequent to HIV-1 infection, expression of these proteins may be modulated by miRNAs. In this figure, line-colors and various interactions with other genes are red Down-regulation, green Up-regulation, beige Regulation, purple Co-expression, brown Physical Interaction, turquoise dotted Predicted Protein Interaction, and mauve dotted Predicted TFactor Regulation (GenePro SA Biosciences, http://www.sabiosciences.com/).

It should be noted that in the GNCPro database, Drp-1 maps to three genes CRMP1, DAPK2, and UTRN. Similarly, the gene IP3R maps to two genes ITPR1 and ITPR3 **[7].** The proteins affected by miRNA-34a are identified as and include IRBIT - inositol 1,4,5-trisphosphate (IP3) receptor-binding protein; AHCYL1 - adenosyl-homocysteinase-like 1; SERP1 - stress-associated endoplasmic reticulum protein 1; SIRT1 - sirtuin 1; NEFM - neurofilament, medium polypeptide; Drp-1 - dystrophin related protein 1/utrophin; CRMP1 - collapsin response mediator protein 1; DAPK2 - death-associated protein kinase 1; UTRN -utropin; ITPR1 - inositol 1,4,5-trisphosphate receptor, type 1; IP3R - inositol 1,4,5-trisphosphate receptor, type 3; ITPR3 - inositol 1,4,5-trisphosphate receptor, type 3; STIM1 - stromal interaction molecule 1; CREB - cAMP responsive element binding protein; and Orai - calcium release-activated calcium modulator **[5, 7-9]**. It should be noted that the Orai gene is absent from the GNCPro database. In addition, it should be noted that the terminology - semantics - is not fully consistent for a few of these proteins across all databases. As mentioned previously, a future analysis of semantics in the public databases will be done **[10].** The figures illustrate various gene interactions among the proteins mentioned above. It is left as a puzzle for the interested reader to identify the various genes and their functions in **Figures 1 & 2 [7-9].**

Acknowledgment:
There are no financial conflicts.

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Citation: **Shapshak,** Bioinformation 8(25): 1243-1244 (2012)