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Interaction between the cellular mRNA and the cellular microRNA linked to human immunodeficiency virus latency

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Summary

[Introduction] MicroRNAs play regulatory roles in a wide variety of cellular events, the regulatory mechanisms of microRNAs (miRs) associated with viral diseases such as human immunodeficiency virus (HIV-1) infection, which is the causative agent of acquired immunodeficiency syndrome (AIDS). However, the role of miRs in HIV infection is largely unknown. In addition, the molecular mechanism of HIV viral latency is not fully understood. Thus, in order to understand the molecular mechanism of viral latency, we have attempted to clarify the role of cellular miR species that are upregulated in the maintenance of viral latency.

[Methods] Based on two previous reports and the data sets of the upregulated cellular miR upon HIV infection, we searched their target cellular mRNAs using an integrated ontology-based rich-text mining algorithm that enables the target identification of miRs. We also analyzed the logical control circuits with regard to the miRs and genes involved in HIV transcription using relational software STRINGS.

[Results] Using the algorithm mentioned above we have identified four cellular gene modules namely: module 1 (cell cycle regulators) APOBEC7G, EIF5, MAPK, MYB, MYC, NCOA3, NKFB1, NFKBA1, P300, RAS, RAF, SRC1; module 2 (cell transcription factors) CREBBP, STAT1, STAT5A; module 3 (HIV-1 transcription modulators) RUNX1, TFCP2, YY1, and; module 4 (immune response genes) IFNA1, IL15, IL6, IL2, IL7, IL10. A high stringency miR target analyses of the 3'-untranslated region (3'-UTR) sequences of these target genes identified common, and multiple in some cases, sequences within these modules. In addition, we have deciphered multiple gene regulatory networks using STRINGS. These regulatory networks were consistent with previous observations.

[Discussion] These findings clearly demonstrate the cross correlations between miR and mRNA in HIV infected cells. Further exploration for the miRs involved in HIV viral replication should

provide us with novel therapeutic approaches with a critical miR network as the target. Development of bio-available measures for introducing specific miR species are vital for novel anti-HIV approaches.