Transcriptomic analysis of HTLV-1 infection in T-cells reveals novel insights into virus-host cell interactions important for virus assembly and infectious spread

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Background:
Virus-host cell interactions are important for HTLV-1 replication and pathogenesis. The details of how these interactions impact virus assembly and cell-to-cell infectious spread represent poorly understood aspects of HTLV-1 biology. To help address this, we have used transcriptomic analysis of infected T-cells in order to provide new insights into HTLV-host cell interactions.

Methods:
We used RNAseq from total RNA extracted from HTLV-1-infected T-cells recovered from co-cultures in order to identify gene expression changes that are due to HTLV-1 infection. Genes identified as differentially expressed by RNAseq that were predicted to be involved in virus replication – particularly particle production and infectious spread – were further investigated by using dsRNA knockdown, immunoblot analysis, and subcellular localization studies.

Results:
We identified 2539 genes that were differentially expressed as a result of virus infection. Two-thirds of the genes identified were found to encode for proteins, over 90 of which have been previously reported to play a role in HTLV-1 replication. PI4K2A and TTC7a were hypothesized to aid in HTLV-1 assembly as RNA knockdown of these genes led to a 50% decrease in HTLV-1 particle production. Both proteins are known to be involved in the synthesis of phosphoinositides that are precursors to phosphatidylinositol 4,5-bisphosphate (PIP2), which enhances Gag targeting to the plasma membrane in infected cells. These and other identified genes are currently under study.

Conclusion:
To date, we have discovered novel genes not previously reported that are differentially expressed in infected T-cells that can impact HTLV-1 replication – including genes that impact the steps involved in virus particle assembly. Ongoing characterization of novel genes dysregulated by HTLV-1 infection seek to define how they influence particle production and infectious cell-to-cell spread.

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