Predictive value of microRNAs for decreasing CD4 T cell count among HIV-1-infected patients who spontaneously control viral replication (HIV controllers)

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Background: A small group of HIV-1-infected individuals (5-15%) control disease progression for several years in the absence of any antiretroviral therapy. Among this group, elite controllers spontaneously control HIV-1 replication (below 50 HIV-1 RNA copies/ml); nevertheless, they are still susceptible to have several aspects of the immune response deregulated, especially elevated immune activation and inflammation. Homeostatic factors contribute to maintain a stable pool of T cells in this situation where T cell apoptosis is enhanced. This situation promotes the release of micro vesicles, such as exosomes that are released by the cells and are present in blood, urine, and saliva. This content includes miRNAs, small non-coding RNA capable of recognizing specific mRNA and inhibiting its translation into proteins. These molecules may thus promote hematopoietic stem cells and regulate the immune system and inflammatory processes that could influence the homeostasis cell equilibrium. HIV could interfere with the exosomal pathway. The direct influence of exosomal miRNAs on the cells of the immune system during HIV infection is a topic that is still poorly understood. Since exosomes can modulate immune responses and may affect HIV pathogenesis, we conducted this cross-sectional study of quantification of selected miRNAs in HIV elite controllers. We also investigated the association of plasma-derived exosome miRNA levels with both soluble cytokine levels and cellular immune activation.

Methods: Two groups of elite controllers were analysed, i.e., those that during the follow up had stable or increasing CD4 T cell count (SEC, N=21), and those who had significant decline of CD4 T cell count (DEC, N=11). Plasma-derived exosomes were used to determine the expression of miRs and determine their association to soluble cytokine markers and cellular immune activation.

Results: Plasma exosome-derived miR-16 and miR-21 are downregulated in DEC group, while miR-221 was upregulated compared to SEC group. Only miR-21 was independently associated with CD4 T cell decline in elite controllers (p=0.049; odds ratio 0.369, IC95 [0.137-0.994]). On the other hand, negative correlation between plasma exosome-derived miR-21 and MCP-1 was found (p=0.020). No correlation between expression of miRs and cellular immune activation markers was found.

Conclusion: Exosome-derived miR-21 might be used as a valuable prognosis soluble biomarker to define HIV-1 elite controllers who will have significant decay in their CD4 T cell counts.

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