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STRIKING CHANGES OF MIRNAS EXPRESSION IN CD4+ T LYMPHOCYTES OCCURRED EVEN IN THE ABSENCE OF AN ESTABLISHED HIV-1 INFECTION

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miRNAs are known to inhibit HIV-1 expression by modulating host innate immunity or by directly interfering with viral mRNAs. Here, we examined miRNA expression in CD4+ T lymphocytes from HIV-1 élite LTNP (éLTNP), naïve, and multiple exposed uninfected individuals (MEU) by real-time PCR-based arrays. Viro-immunological analysis in CD4+ T cells revealed that éLTNP had a lower amount of activated T lymphocytes, less activated regulatory T cells, more TREC+ cells, and less HIV-DNA than naïve patients. Among the quantified 377 miRNAs, 113 varied (either up or down) of at least 1 Log_{10} between each patients group and healthy controls: 25 miRNAs were up-regulated, while 88 were down-regulated. All the up-regulated miRNAs were undetectable in cells from controls. In all patients' classes, 3 miRNAs (miR-203, miR-449a, miR-502-5p) were up-regulated and 5 (miR-329, miR-337-5p, miR-379, miR-503, miR-518d-3p) were down-regulated, suggesting a hypothetic HIV-1 exposure signature. By hierarchical clustering, éLTNP clustered with naïve whereas all MEU grouped together, supporting that miRNAs may work as HIV-1-related genetic factors. Furthermore, 21 miRNAs significantly differentiated éLTNP from MEU and 23 miRNAs the naïve from MEU (16 miRNAs were in common), only miR-155 characterized éLTNP vs. naïve. Among these miRNAs, only 3 were involved in viral replication (let-7a, miR-34a, miR-485-3p), whereas 5 in immune response (miR-21, miR-23a, miR-125-3p, miR-155, miR-424). On the whole, these findings suggest that miRNA profile observed in all HIV-1+ and MEU subjects could be the result not only of a productive infection, but also of the exposure to viral products (e.g., plasma gp120 that can unspecifically bind CD4+ T cells). Thus, even the exposure to HIV products can leave stable signs in immune cells, whose meaning has to be clarified.