Daily Immunological/Virological Variations in Aviremic ART-treated HIV Participants

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BACKGROUND

Biological functions fluctuate in a circadian manner to align with environmental changes. In healthy uninfected individuals, variations in T-cell trafficking are documented in the blood, with nadir CD4 counts in the morning. Daily variations are also observed for plasma cortisol and melatonin, two regulators of immune functions. HIV infection is associated with pronounced alterations in CD4 T-cell homeostasis and chronic immune activation. HIV transcription is regulated by BMAL1, a circadian clock master regulator. However, daily variations in immunological/virological parameters during ART-treated HIV infection remain unknown.

METHODS

ART-treated people living with HIV (PLWH; median CD4 counts: 606 cells/ml; age: 57 years; time since infection: 242 months; aviremia under ART: 216 months) were hospitalized at the CRCHUM Phase I Clinic a Friday afternoon for 40 hours. Starting the next morning, blood was collected/processed every 4 hours for 24 hours before food intake. Polychromatic flow cytometry allowed cell counting/phenotypic analysis on fresh blood. Plasma levels of cortisol/melatonin and markers of mucosal barrier impairment (FABP2, LBP) were measured by ELISA. PBMC were frozen. HIV DNA/RNA were quantified by PCR on sorted CD4+ T-cells.

RESULTS

Study cohort I clinical parameters

<table>
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<tr>
<th>Group</th>
<th>Sex</th>
<th>Age (years)</th>
<th>CD4 T cell count</th>
<th>CD8 T cell count</th>
<th>Plasma cortisol</th>
<th>Time since infection</th>
<th>Time since ART initiation</th>
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Experiment protocol

Wake 10:00  Dim Light  Sleep 22:00

Blood Sampling

1. Plasma soluble factor quantification
2. PBMC immunological/virological measurements

Circadian Variations in Plasma Markers

CONCLUSIONS

Daily variations in the blood T-cell/myeloid compartments, mucosal permeability markers, HIV transcription, and melatonin/cortisol levels, were observed in a cohort of aviremic ART-treated PLWH. These findings provide a rationale for studying the role of the circadian clock machinery in regulating residual HIV transcription under ART.

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