ELEVATED CELL-ASSOCIATED HIV-1 RNA TRANSCRIPTS PREDICT LATER BLIPS

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Background:
Virally suppressed HIV patients on (vsART) occasionally experience plasma viral load blips, whose clinical significance is increasingly being recognised. Recently we showed a cross-sectional correlation between previous blips and high levels of cell-associated (CA)-HIV-1 RNA transcripts. Herein, we prospectively studied whether higher CA-HIV-RNA increases the likelihood of subsequent blips.

Methods:
Blood (3 mls) from 61 HIV-1 vsART patients, who had in the 2 years prior either 1 or 2 blips (n = 32), or no blips (n=29) was collected. RNA was extracted from white blood cells for analysis at Time-0, and cell-associated (CA)-HIV-RNA transcripts measured using the previously described πCode assay. Any further blips over the next 2 years were then monitored (between Time-0 and +2 years). Logistic regression was used to predict any future blip within two years. A cut-off value was determined using the Youden's index with Receiver operator characteristic (ROC) curves.

Results:
30 subjects had blips and 31 did not over the 2 years after CA-HIV-RNA analysis. Individuals with blip within the previous 2 years had significantly higher levels of CA-HIV-RNA transcripts vs without blip (median 169 vs 20 copies/10^6 white blood cells; $p<0.0001$). ROC analysis identified CA-HIV-RNA, above a cut-off of 64 copies/10^6 cells, predicted a later blip with 70.0% sensitivity, 90.3% specificity with Area Under the Curve (AUC) of 0.858 ($p<0.0001$). CA-HIV-RNA was strongly associated with increased probability of a future blip within 2 years (Odds Ratio: OR 13.9, 95% CI 3.7 to 52.5, $p < 0.001$) per ten-fold increase in CA-HIV-RNA. Previous blips within 2 years before Time-0, showed a moderate but non-significant association for future blip (OR 1.8, 95% CI 0.66 to 5.13, $p=0.248$), compared to prior non-blip status.

Conclusion:
Despite vsART, higher CA-HIV-RNA transcripts are strongly associated with risk of subsequent blips and imply current active viral replication.

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