HTLV-1 expression reduces local chromatin looping

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Background:
A typical HTLV-1-infected individual persistently carries >10^4 different clones, each with a single-copy provirus integrated in a unique genomic site. Using our quantitative circular chromosome conformation capture (q4C) method (Melamed, Yaguchi et al, elife 2018) we previously showed that the provirus forms abnormal chromatin loops with the flanking host DNA; the number and distribution of the contacts depends on the proviral integration site. The presence of these contacts was frequently associated with the presence of a host-encoded CTCF binding site. We also showed both adjacent and distal dysregulation of transcription from the infected chromosome. However, it remained unclear whether these effects were exerted simply by the presence of the provirus or by its transcription.

Methods:
T-cell clones, naturally infected by HTLV-1 and each carrying a single HTLV-1 provirus, were sorted by flow cytometry according to Tax expression. T cell clones expressing GFP in response to Tax expression were also used. q4C was performed to analyse chromatin looping in the Tax-expressing and non-expressing cells. RNA-sequencing was used to quantify host expression around the integration site in the sorted population.

Results:
We identified a median of 6.5 contacts per clone between the provirus and flanking host chromatin in the non-Tax-expressing cells. This number fell to a median of 0 contacts per clone in the Tax-expressing cells ($p = 0.03$, paired Wilcoxon test). The peak density and mean peak height were also both significantly lower in the Tax-expressing cells ($p < 0.0001$, Wilcoxon test). This difference was particularly strong in the host genome downstream of the integration site.

Conclusion:
We conclude that plus-strand expression of HTLV-1 is accompanied by temporary removal of local chromatin loops between the provirus and the flanking host genome.

Disclosure of Interest Statement:
Authors declare that they have no competing interests