# Selective clonal persistence of HTLV-1 in vivo: radial chromatin organization, integration site and host transcription

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**Background:**
Individuals infected with the human T-cell leukaemia virus HTLV-1 have of the order of $10^3$-$10^6$ clones of infected T cells, each clone defined by the unique genomic integration site (IS) of the single-copy HTLV-1 provirus. HTLV-1 integrates into the genome at a frequency proportional to chromosome size. But in vivo, we previously showed selective persistence of HTLV-1+ T-cell clones that carry the provirus in an acrocentric chromosome (chromosomes 13, 14, 15, 21, 22). We postulated that this selective persistence is due to the known association of the acrocentric chromosomes with the transcriptionally repressive environment of the nucleolar periphery.

**Methods:**
To test the hypothesis that HTLV-1 persistence in vivo depends on the intranuclear position of the provirus, we compared the genomic location of >230,000 IS of HTLV-1 from in vitro infection with that of >160,000 IS identified in peripheral blood mononuclear cells of individuals persistently infected with HTLV-1. We aligned these IS data with the data reported by Chen et al (2018) from their novel technique of tyramide signal amplification-sequencing (TSA-seq), which these authors used to measure the physical distance between each genomic region and specific intranuclear sites, namely the nuclear lamina and nuclear speckles. Additionally, we aligned HTLV-1 IS data against chromatin accessibility, chromatin modifications and the intensity of host transcription in the flanking genome.

**Results:**
We found that whereas certain epigenetic marks were weakly associated with clone survival, three factors independently explained >40% of the observed variance in clone survival of HTLV-1 in vivo: the radial intranuclear position of the provirus, the absolute genomic distance of the provirus from the centromere, and the intensity of host genome transcription flanking the provirus.

**Conclusion:**
Clonal persistence of HTLV-1 in vivo is favoured not only by transcriptional repression, but also by the spatial position of the provirus in specific sites in the nucleus.

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