CHARACTERIZATION OF HIV-1 LATENT RESERVOIR IN CIRCULATING CD4$^+$ T CELLS IN RALTEGRAVIR-TREATED PATIENTS

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Background:
Raltegravir is an integrase inhibitor, and the failed-to-inhibit HIV DNA would be circularized by host cell DNA ligase. The PINT study was a pilot trial that recruited 8 primary-infection and 8 chronic-infection patients, and the participants were prescribed with Raltegravir and Truvada in a 3-year therapy. The hypothesis was Raltegravir would change the distribution and characteristics of the HIV DNA in circulating CD4$^+$ T cells in the patients.

Methods:
We separated 4 CD4$^+$ T cell subsets by flow cytometry sorting, then amplified and sequenced the near full-length HIV-1 DNA from the sorted subsets. We also characterized the sequences to determine whether they are linear or circularized by using a duplex-PCR method that targets the 2-LTR junction. The sequences were categorized based on their intactness and phylogeny analyses were performed.

Results:
Full-length sequences have been generated from CD4$^+$ T cells from 6 participants (Chronic arm=3, Primary arm=3). Primary infection group has a higher similarity in sequences across all timepoints and subsets compared to chronic group. Base on preliminary phylogeny results, neither groups demonstrated considerable evolution in sequences.

Conclusion:
Based on current analyses, the trial did limit the evolution of viral DNA in patients, suggesting the diversity is driven by clonal expansion. Further phylogenetic analyses are required especially focusing on comparing the circularized versus linear HIV DNA, and the replication-competent versus defected HIV DNA.

Disclosure of Interest Statement:
The PINT study was in collaboration with Merck Sharp & Dohme LLC. Project funding was provided by NIH. There was collaboration regarding sequence analyses with WIMR, Westmead Hospital.