

## PE8

### Purging HIV-1 from latent reservoirs using human methyltransferase inhibitors

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**Background:** Histone lysine methylation is one of the most robust histone modifications, with central role in conferring epigenetic control to the chromatin template. Latent HIV proviruses are silenced as a result of deacetylation and methylation of histones located at the long terminal repeats (LTRs). Thus the chromatin remodeling plays a major role in chromatin-mediated repression or expression of the HIV-1 promoter. Here, we evaluated the potential of two histone methyl transferase inhibitors (HMTIs) namely Chaetocin and BIX-01294 in reactivating HIV-1 from latency.

**Methods:** We used CD8T-cells depleted PBMCs isolated from 15 HIV+ HAART-treated patients with undetectable viral load over a period 4 years. We measured HIV-1 recovery in ex-vivo cell cultures first activated by PHA for one day and then treated with chaetocin and BIX-01294 and cultivated in RPMI medium supplemented with IL-2 and fetal bovine serum while CD8+ T-cells depleted PBMCs activated with PHA and then cultivated in RPMI medium supplemented with IL-2 and fetal bovine serum were used as control samples.

**Results:** HMTIs induced purging in 11 out of 15 subjects. Second day after treatment with the drugs, culture supernatants were tested for viral load using qPCR and the results revealed HIV-1 emergence from day 3rd -day 29th (median 09 days) with viral load from 2.2 log<sub>10</sub> to 6.0 log<sub>10</sub> (median of 5.7). To find a correlation between PBMC proviral load and culture positivity, qPCR was done. Proviral load varied from 28.51 to 515.90 (median=91; mean=144.21). The results showed that culture positivity is independent of proviral load, CD4+T cell nadir, time of viral load below detection limits and antiretroviral scheme.

**Conclusions:** As part of an attempt to HIV eradication in human hosts, it would be important to overcome HIV latency, one of the major obstacles towards the sterilizing HIV cure. We showed here that these non-administrable HMTIs may provide a therapy to purge the dormant HIV-1 from reservoirs possibly in combination with other chromatin remodeling drugs. Therefore, clinical grade HMTIs should be synthesized or screened and evaluated to exploit their HIV reactivation potential.