

MEASUREMENT OF TOTAL AND INTEGRATED HIV DNA MAY BE A USEFUL INDICATOR OF ONGOING REPLICATION

Mexas AM, Liszewski MK, Graf EH, Yu JJ, and O'Doherty U

Department of Pathology and Laboratory Medicine, University of Pennsylvania, 265 John Morgan Building, 3620 Hamilton Walk, Philadelphia, PA 19104

Introduction: How HIV reservoirs are maintained on apparently suppressive HAART remains unclear. One theory is that reservoirs form early after infection and are maintained in the absence of ongoing replication. Alternatively, ongoing replication may occur at a low level that is not easy to detect. Either way monitoring reservoir size and ongoing replication would be a useful way to monitor therapies that aim to intensify anti-viral activity or aim to push out reservoirs. Here we present data that suggest that monitoring the ratio of total to integrated DNA may enable us to monitor ongoing replication.

Methods: We developed a sensitive, precise assay to measure HIV integration. We then validated this technique and demonstrated that it is accurate using a complimentary method. With the knowledge that we measure integration accurately, we can now determine the ratio of total and integrated HIV DNA to estimate the extent of unintegrated HIV present in patient samples.

Results: In patients off HAART, we always find an excess of unintegrated DNA. Surprisingly, in patients on HAART, there is a range of levels of excess unintegrated HIV DNA. We note in two patients with a history of model adherence and undetectable viral loads, total DNA approaches the level of integrated HIV DNA.

Conclusions: Our data suggest that the presence of an excess of unintegrated HIV DNA may indicate ongoing replication on HAART. We suggest that monitoring the ratio of total to integrated HIV DNA over time may be a useful method to determine the extent of ongoing replication in patient samples.