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Tin Phan* (tin.t.phan@asu.edu), Yang Kuang, Maria Emelianenko, Daniel M Anderson, Fatah Kashanchi, Catherine Demarino, Michelle L Pleet, Daniel O Pinto and Maria Cowen. Differences in Transcriptional Dynamics Between T-cells and Macrophages as Determined by a Three-State Mathematical Model.

The treatment of HIV-1 with the use of combination antiretroviral therapy greatly reduced viral loads. Yet, viral transcription persists despite treatment. We created and validated a three-state mathematical model to explore the states of the HIV-1 LTR and generation of viral products. This model is novel in its integration of long and short HIV-1 RNA products and can be used to successfully model different cell types in a variety of physiological conditions.

We demonstrated that the overall patterns of change in LTR states are similar in T-cells and macrophages. However, both cell types exhibit unique LTR dynamics in terms of timing, relative proportion of LTR states, and differences in LTR state variability. These variations result in differences in the magnitude of viral products generated in infected T-cells and macrophages. The model can provide a reasonable match for the experimental data without any computational fitting techniques.

Through incorporation of transcription inhibitor into the model, we showed how to implement the model to assess drug efficacy among cell types. Furthermore, the model provides a platform to study various transcriptional dynamics. (Received September 25, 2018)