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Researchers identify the source of 'noise' in HIV

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New research identifies a molecular mechanism that the human immunodeficiency virus (HIV) appears to utilize for generating random fluctuations called "noise" in its gene expression. The study, published by Cell Press in the April 20th issue of the *Biophysical Journal,* pinpoints the likely source of HIV gene-expression noise and provides intriguing insight into the role of this noise in driving HIV's fate decision between active replication and latency.

After infecting a human cell, HIV integrates into the genome and typically begins to actively replicate. However, the virus can also enter a long-lived latent state, which remains the greatest barrier to eradicating virus from the patient. Senior study author, Dr. Leor S. Weinberger, a molecular virologist and systems biologist from the Department of Chemistry and Biochemistry at the University of California, San Diego, recently showed that noise in HIV gene-expression critically influences the viral decision to enter either active replication or latency. However, the source of the noise was not clear.

To probe the source of this inherent noise in HIV gene expression, Dr. Abhyudai Singh working in Dr. Weinberger's laboratory exploited a technique from electrical engineering that analyzes how noise changes across different levels of expression. The researchers examined cells carrying a single integrated copy of HIV engineered to produce a quantifiable protein, and measured HIV-1 expression noise at dozens of different viral integration sites which act as distinct genetic environments for viral gene expression.

Surprisingly, the authors find that HIV noise levels are substantially higher than measured in other organisms, and that HIV gene expression occurs in randomly timed bursts. During these expression bursts multiple copies of HIV gene products are produced which leads to the high noise levels in HIV gene expression. The bursting model argues that during active expression HIV cycles between periods of silence and bursting and provides insight into how HIV may be activated by host signaling molecules.

"We know that noise in gene-expression can critically influence HIV's entry to proviral latency. These new results point to transcriptional bursting as a major source of the noise" says Dr. Weinberger. "This finding that transcriptional bursting generates an exceptionally noisy HIV promoter, noisier than almost all other measured promoters, supports the theory that latency may be fundamental to the HIV life cycle and that HIV evolved for probabilistic entry into latency."

More information: Weinberger et al.: "Transcriptional bursting from the HIV-1 promoter is a significant source of stochastic noise in HIV-1 gene expression." The Biophysical Journal, April, 2010. www.biophysics.org/

Provided by Cell Press