A036 · Systematic Identification and Characterization of Transcriptional Silencers Across Viral Genomes

Presenter: Mohamed Yousry ElSadec — Bioinformatics Program, Boston University

Authors: Mohamed Yousry ElSadec, Benedetta D'Elia, Tommy Taslim, Susan Kales, Ryan Tewhey, Juan I. Fuxman Bass

Session: Day 1 · Thu Oct 1, 2026 · 2:15–4:15 PM

Precise and tunable control of gene expression depends on both activating and repressive mechanisms. While promoters and enhancers have been extensively characterized, silencers remain comparatively understudied despite their essential roles in transcriptional repression, dosage control, and safeguarding against inappropriate gene activation. Previous work from our group showed that viral genomes are enriched for activating cis-regulatory elements, suggesting that a complementary repressive layer must exist to maintain transcriptional balance within these compact genomes. Moreover, stage-specific control of gene activation and repression is critical for viral persistence and the ordered progression of the lytic expression cascade. To systematically identify viral silencers, we performed Massively Parallel Reporter Assays (MPRA) tiling the genomes of 34 double-stranded DNA viruses and retroviruses across multiple promoter contexts and cell lines. We observed a high density of silencers distributed throughout most viral genomes. These elements frequently cluster near activating regions, are often compact, and exhibit diverse transcription factor motif signatures. Some silencers act in a promoter- or cell-specific manner, while others are broadly repressive; a subset are bifunctional, switching between repression and activation depending on context. Motif enrichment analysis revealed that while many viral silencers share transcription factors with human silencers, others appear to be regulated by distinct sets of transcription factors. Together, this work delivers the first systematic atlas of transcriptional silencers across viral genomes, revealing a pervasive and previously unappreciated repressive regulatory layer that shapes viral gene-expression programs.

Systematic Identification and Characterization of Transcriptional Silencers Across Viral Genomes

Mohamed Yousry ElSadec[1]*, Benedetta D'Elia[2], Tommy Taslim[2], Susan Kales[3], Ryan Tewhey[3], Juan I Fuxman Bass[1,2]

[1]Bioinformatics Program, Boston University, Boston, MA 02215, USA, [2]Molecular Biology, Cell Biology and Biochemistry Program, Boston University, Boston, MA 02215, USA, [3]The Jackson Laboratory, Bar Harbor, ME 04609, USA.

Precise and tunable control of gene expression depends on both activating and repressive mechanisms. While promoters and enhancers have been extensively characterized, silencers remain comparatively understudied despite their essential roles in transcriptional repression, dosage control, and safeguarding against inappropriate gene activation. Previous work from our group showed that viral genomes are enriched for activating cis-regulatory elements, suggesting that a complementary repressive layer must exist to maintain transcriptional balance within these compact genomes. Moreover, stage-specific control of gene activation and repression is critical for viral persistence and the ordered progression of the lytic expression cascade. To systematically identify viral silencers, we performed Massively Parallel Reporter Assays (MPRA) tiling the genomes of 34 double-stranded DNA viruses and retroviruses across multiple promoter contexts and cell lines. We observed a high density of silencers distributed throughout most viral genomes. These elements frequently cluster near activating regions, are often compact, and exhibit diverse transcription factor motif signatures. Some silencers act in a promoter- or cell-specific manner, while others are broadly repressive; a subset are bifunctional, switching between repression and activation depending on context. Motif enrichment analysis revealed that while many viral silencers share transcription factors with human silencers, others appear to be regulated by distinct sets of transcription factors. Together, this work delivers the first systematic atlas of transcriptional silencers across viral genomes, revealing a pervasive and previously unappreciated repressive regulatory layer that shapes viral gene-expression programs.