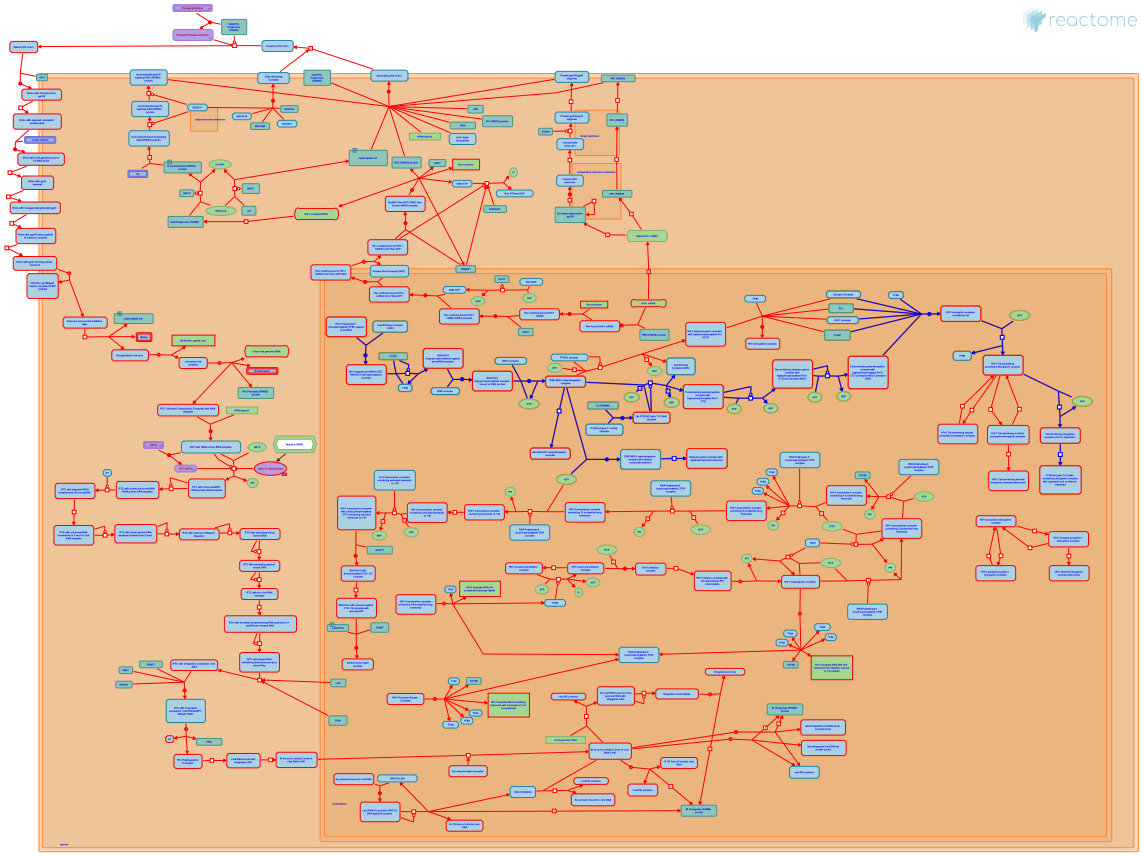
HIV Transcription Elongation



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.
The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

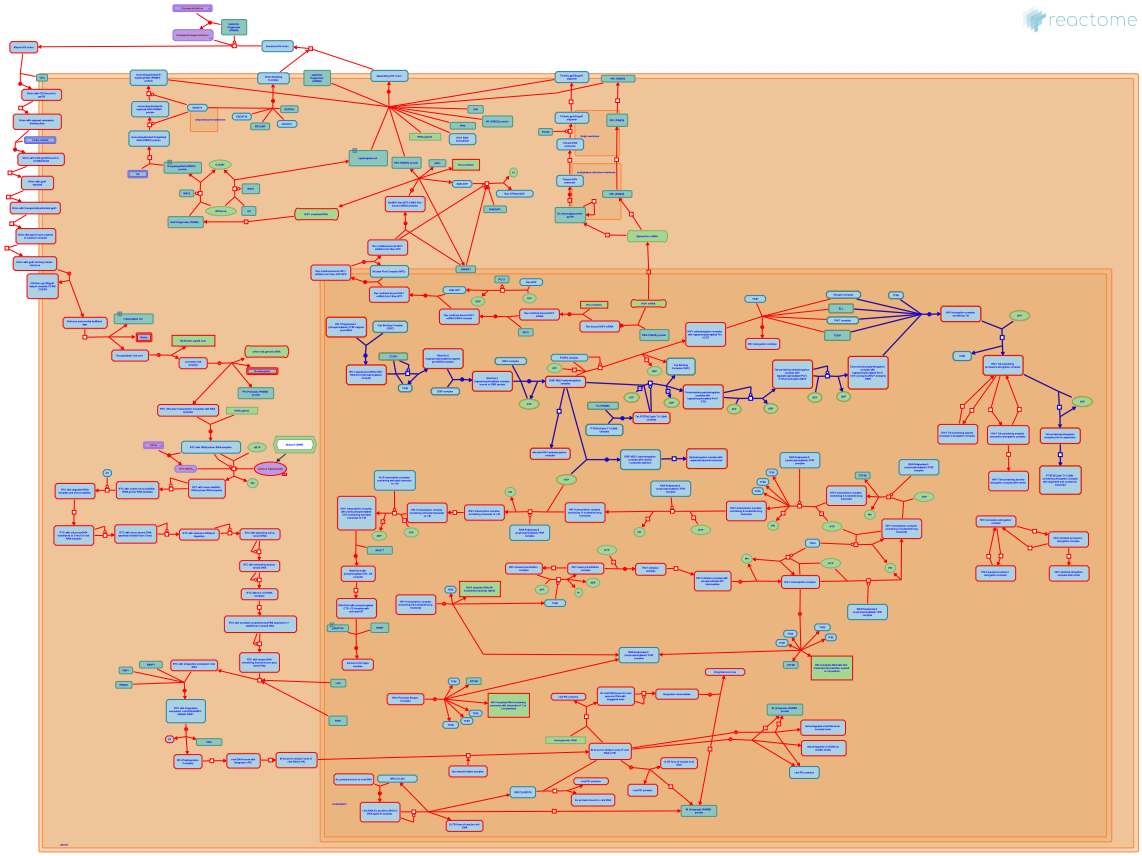
HIV Transcription Elongation ↗

Stable identifier: R-HSA-167169

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: RNA Polymerase II Transcription Elongation (Homo sapiens)



In the absence of the HIV-1 protein Tat, transcription of the proviral DNA is inefficient and results in the production of truncated transcripts (Kao et al., 1987). While initiation of transcription from the HIV-1 LTR and formation of the early elongation complex occurs normally, transcription elongation is incomplete with non-processive polymerases disengaging from the proviral DNA template prematurely (reviewed in Karn 1999). The mechanism of Tat-mediated elongation is described below.

Literature references

Karn, J. (1999). Tackling Tat. *J Mol Biol, 293*, 235-54. ↗

Herrmann, CH., Rice, AP. (2003). Regulation of TAK/P-TEFb in CD4+ T lymphocytes and macrophages. *Curr HIV Res, 1*, 395-404. ↗

Editions

2005-07-27	Authored	Matthews, L., Rice, AP.
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Formation of the HIV-1 Early Elongation Complex ↗

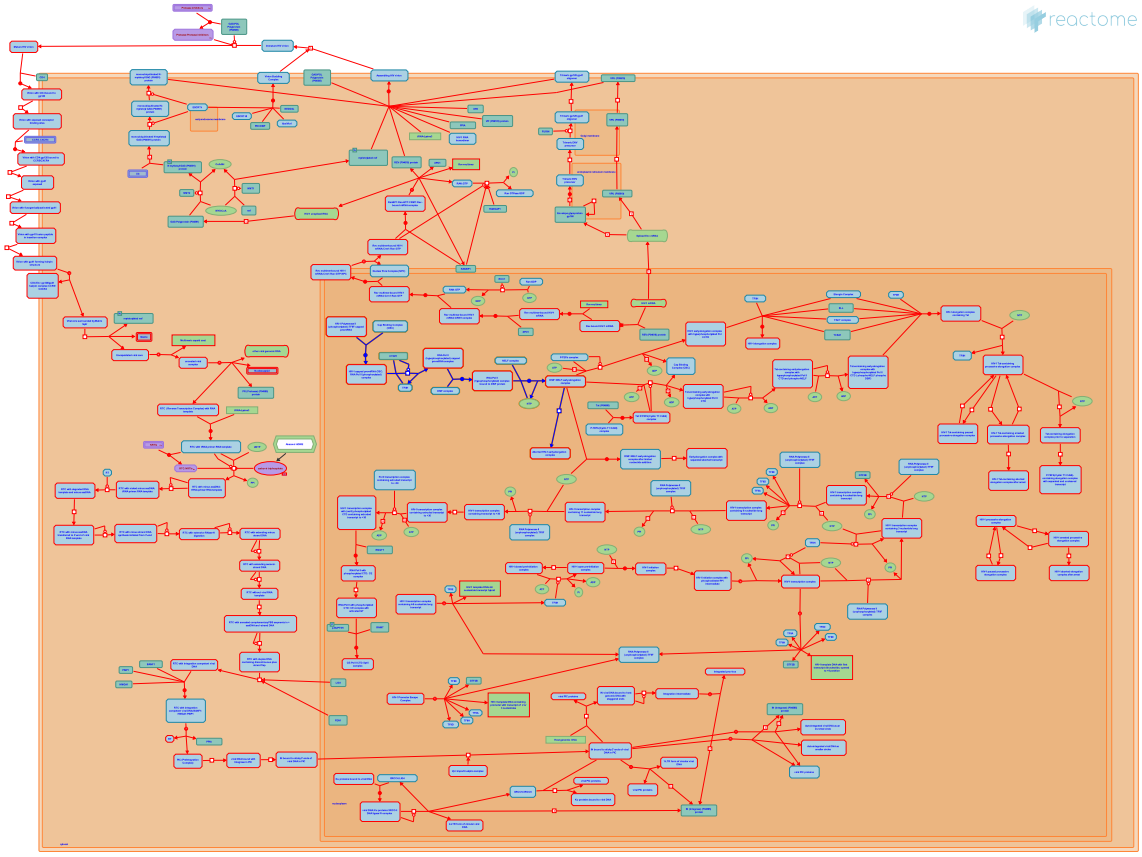
Location: HIV Transcription Elongation

Stable identifier: R-HSA-167158

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Formation of the Early Elongation Complex (Homo sapiens)



This HIV-1 event was inferred from the corresponding human RNA Poll II transcription event. The details relevant to HIV-1 are described below. Formation of the early elongation complex involves hypophosphorylation of RNA Pol II CTD by FCP1P protein, association of the DSIF complex with RNA Pol II, and formation of DSIF:NELF:HIV-1 early elongation complex as described below (Mandal et al 2002; Kim et al 2003; Yamaguchi et al 2002).

Literature references

Furuya, A., Sato, H., Kim, DK., Yamada, T., Wada, T., Handa, H. et al. (2003). Structure-function analysis of human Spt4: evidence that hSpt4 and hSpt5 exert their roles in transcriptional elongation as parts of the DSIF complex. *Genes Cells, 8*, 371-8. ↗

Mandal, SS., Reinberg, D., Cabane, K., Cho, H., Kim, S. (2002). FCP1, a phosphatase specific for the heptapeptide repeat of the largest subunit of RNA polymerase II, stimulates transcription elongation. *Mol Cell Biol, 22*, 7543-52. ↗

Wada, T., Handa, H., Inukai, N., Narita, T., Yamaguchi, Y. (2002). Evidence that negative elongation factor represses transcription elongation through binding to a DRB sensitivity-inducing factor/RNA polymerase II complex and RNA. *Mol Cell Biol, 22*, 2918-27. ↗

Editions

2005-07-27	Authored	Matthews, L., Rice, AP.
2005-07-27	Edited	Matthews, L.

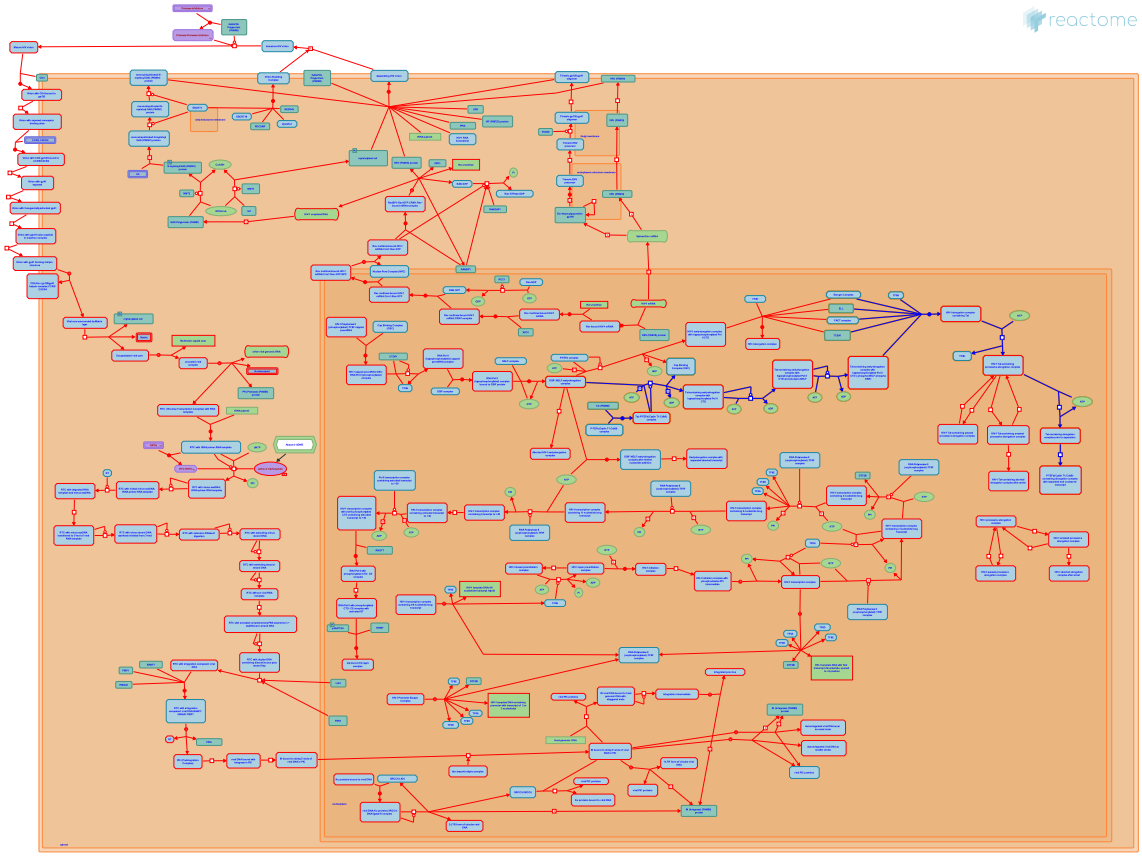
Tat-mediated elongation of the HIV-1 transcript ↗

Location: HIV Transcription Elongation

Stable identifier: R-HSA-167246

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease



The Tat protein is a viral transactivator protein that regulates HIV-1 gene expression by controlling RNA Pol II-mediated elongation (reviewed in Karn 1999; Taube et al. 1999; Liou et al. 2004; Barboric and Peterlin 2005). Tat appears to be required in order to overcome the arrest of RNA Pol II by the negative transcriptional elongation factors DSIF and NELF (Wada et al. 1998; Yamaguchi et al. 1999; Yamaguchi et al 2002; Fujinaga et al. 2004). While Pol II can associate with the proviral LTR and initiate transcription in the absence of Tat, these polymerase complexes are non-processive and dissociate from the template prematurely producing very short transcripts (Kao et al. 1987). Tat associates with the RNA element, TAR, which forms a stem loop structure in the leader RNA sequence (Dingwall et al. 1989). Tat also associates with the cellular kinase complex P-TEFb(Cyclin T1:Cdk9) and recruits it to the TAR stem loop structure (Herrmann, 1995) (Wei et al. 1998). This association between Tat, TAR and P-TEFb(Cyclin T1:Cdk9) is believed to bring the catalytic subunit of this kinase complex (Cdk9) in close proximity to Pol II where it hyperphosphorylates the CTD of RNA Pol II (Zhou et al. 2000). The RD subunits of NELF and the SPT5 subunit of DSIF, which associate through RD with the bottom stem of TAR, are also phosphorylated by P-TEFb(Cyclin T1:Cdk9) (Yamaguchi et al. 2002; Fujinaga et al. 2004; Ivanov et al. 2000). Phosphorylation of RD results in its dissociation from TAR. Thus, Tat appears to facilitate transcriptional elongation of the HIV-1 transcript by hyperphosphorylating the RNA Poll II CTD and by removing the negative transcription elongation factors from TAR. In addition, there is evidence that the association of Tat with P-TEFb(Cyclin T1:Cdk9) alters the substrate specificity of P-TEFb enhancing phosphorylation of ser5 residues in the CTD of RNA Pol II (Zhou et al. 2000).

Literature references

Peterlin, BM., Barboric, M. (2005). A new paradigm in eukaryotic biology: HIV Tat and the control of transcriptional elongation. *PLoS Biol, 3*, e76. ↗

Skinner, MA., Karn, J., Green, SM., Singh, M., Ernberg, I., Dingwall, C. et al. (1989). Human immunodeficiency virus 1 tat protein binds trans-activation-responsive region (TAR) RNA in vitro. *Proc Natl Acad Sci U S A, 86*, 6925-9. ↗

Peterlin, BM., Irwin, D., Taube, R., Huang, Y., Fujinaga, K., Kurosu, T. (2004). Dynamics of human immunodeficiency virus transcription: P-TEFb phosphorylates RD and dissociates negative effectors from the transactivation response element. *Mol Cell Biol, 24*, 787-95. ↗

Karn, J. (1999). Tackling Tat. *J Mol Biol, 293*, 235-54. ↗

Gaynor, RB., Kwak, YT., Ivanov, D., Guo, J. (2000). Domains in the SPT5 protein that modulate its transcriptional regulatory properties. *Mol Cell Biol, 20*, 2970-83. ↗

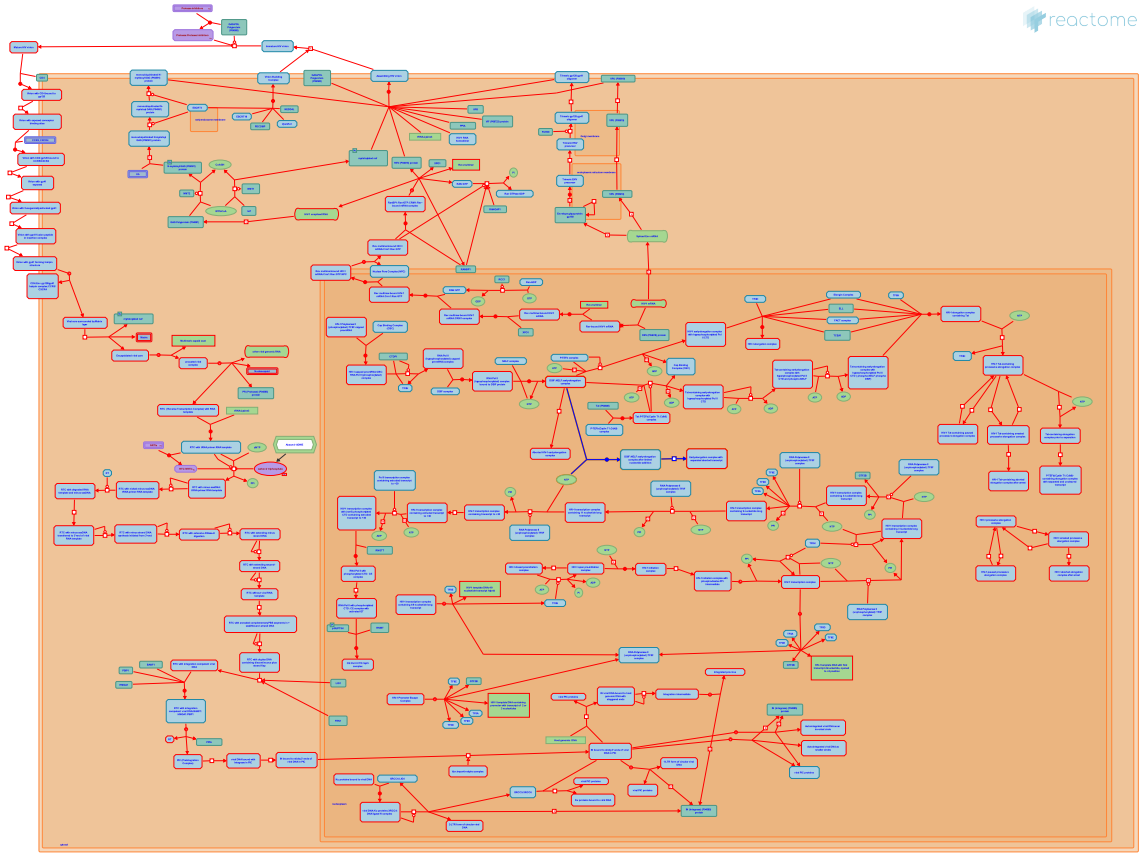
Abortive elongation of HIV-1 transcript in the absence of Tat ↗

Location: HIV Transcription Elongation

Stable identifier: R-HSA-167242

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease



This event was inferred from the corresponding Reactome human Poll II transcription elongation event. The details specific to HIV-1 transcription elongation are described below. In the absence of the HIV-1 Tat protein, the RNA Pol II complexes associated with the HIV-1 template are non-processive. RNA Pol II is arrested after promoter clearance by the negative transcriptional elongation factors DSIF and NELF as occurs during early elongation of endogenous templates (Wada et al, 1998; Yamaguchi et al. 1999). This arrest cannot be overcome by P-TEFb mediated phosphorylation in the absence of Tat however, and elongation aborts resulting in the accumulation of short transcripts (Kao et al., 1987).

Literature references

Peterlin, BM., Luciw, PA., Kao, SY., Calman, AF. (1987). Anti-termination of transcription within the long terminal repeat of HIV-1 by tat gene product. *Nature, 330*, 489-93. ↗

Takagi, T., Buratowski, S., Yano, K., Ferdous, A., Wada, T., Handa, H. et al. (1998). DSIF, a novel transcription elongation factor that regulates RNA polymerase II processivity, is composed of human Spt4 and Spt5 homologs. *Genes Dev, 12*, 343-56. ↗

Takagi, T., Yano, K., Furuya, A., Wada, T., Handa, H., Hasegawa, J. et al. (1999). NELF, a multisubunit complex containing RD, cooperates with DSIF to repress RNA polymerase II elongation. *Cell, 97*, 41-51. ↗

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