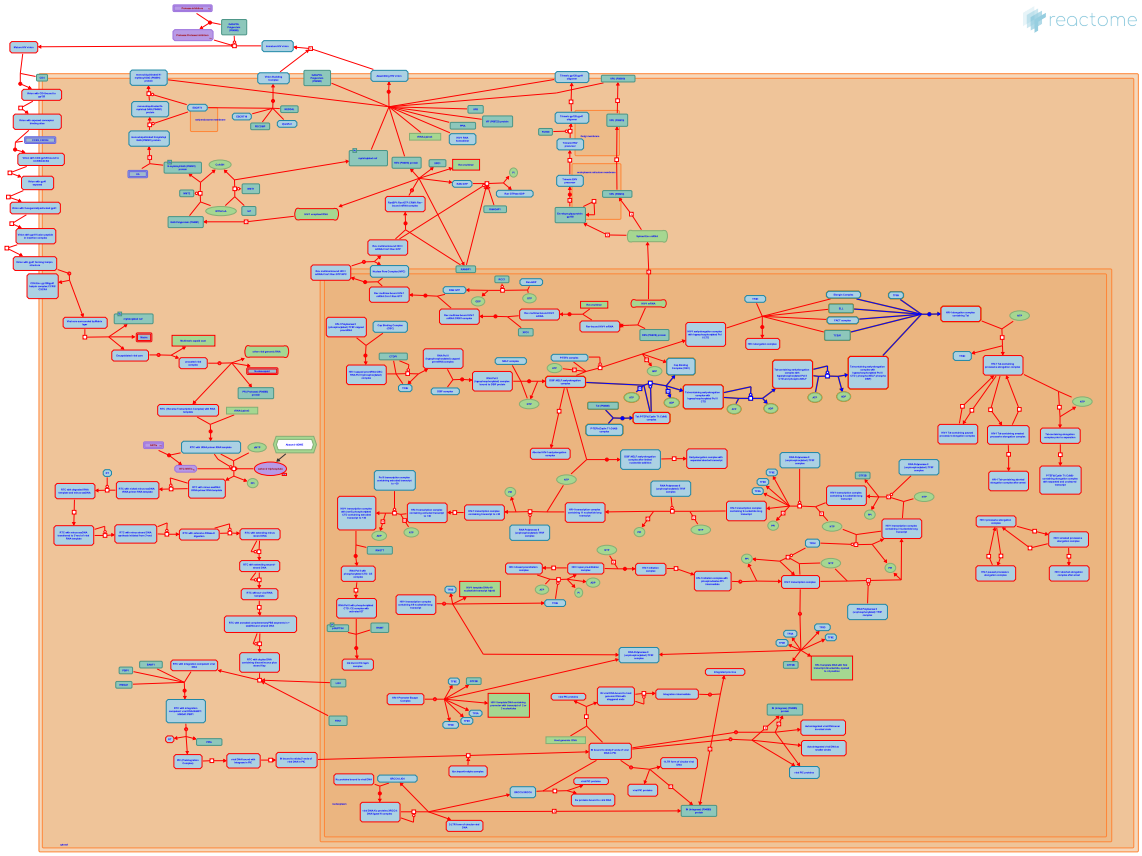
Formation of HIV-1 elongation complex containing HIV-1 Tat



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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. ↗

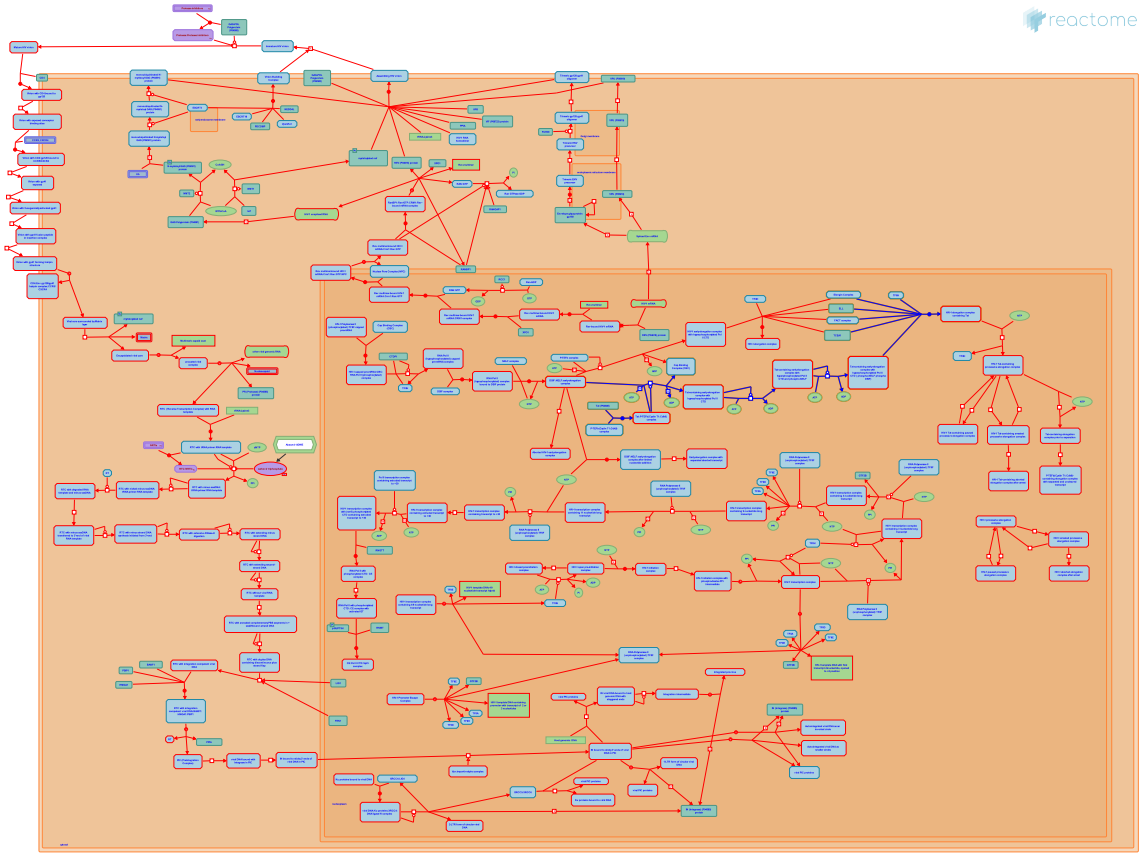
Formation of HIV-1 elongation complex containing HIV-1 Tat ↗

Stable identifier: R-HSA-167200

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Formation of RNA Pol II elongation complex (Homo sapiens)



This HIV-1 event was inferred from the corresponding human RNA Poll II transcription event in Reactome. The details relevant to HIV-1 are described below. For a more detailed description of the general mechanism, see the link to the corresponding RNA Pol II transcription event below. The formation of the HIV-1 elongation complex involves Tat mediated recruitment of P-TEFb(Cyclin T1:Cdk9) to the TAR sequence (Wei et al, 1998) and P-TEFb(Cyclin T1:Cdk9) mediated phosphorylation of the RNA Pol II CTD as well as the negative transcriptional elongation factors DSIF and NELF (Herrmann, 1995; Ivanov et al. 2000; Fujinaga et al. 2004; Zhou et al., 2004).

Literature references

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. ↗

Rice, AP., Herrmann, CH. (1995). Lentivirus Tat proteins specifically associate with a cellular protein kinase, TAK, that hyperphosphorylates the carboxyl-terminal domain of the large subunit of RNA polymerase II: candidate for a Tat cofactor. *J Virol, 69*, 1612-20. ↗

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. ↗

Wei, P., Jones, KA., Fang, SM., Fischer, WH., Garber, ME. (1998). A novel CDK9-associated C-type cyclin interacts directly with HIV-1 Tat and mediates its high-affinity, loop-specific binding to TAR RNA. *Cell, 92*, 451-62. ↗

Kashanchi, F., Brady, JN., Deng, L., Park, HU., Zhou, M., Pumfery, A. et al. (2004). Coordination of transcription factor phosphorylation and histone methylation by the P-TEFb kinase during human immunodeficiency virus type 1 transcription. *J Virol, 78*, 13522-33. ↗

Editions

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Association of Tat with P-TEFb(Cyclin T1:Cdk9) ↗

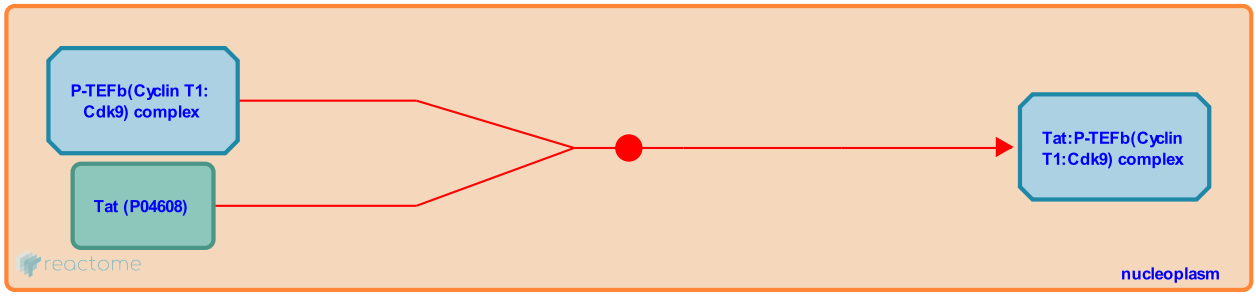
Location: Formation of HIV-1 elongation complex containing HIV-1 Tat

Stable identifier: R-HSA-167234

Type: binding

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease



Tat associates with the Cyclin T1 subunit of P-TEFb (Cyclin T1:Cdk9) through a region of cysteine-rich and core sequences referred to as the ARM domain within Tat (Wei et al., 1998; see also Herrmann 1995). This interaction is believed to involve metal ions stabilized by cysteine residues in both proteins (Bieniasz et al., 1998; Garber et al., 1998).

Literature references

Rice, AP., Herrmann, CH. (1995). Lentivirus Tat proteins specifically associate with a cellular protein kinase, TAK, that hyperphosphorylates the carboxyl-terminal domain of the large subunit of RNA polymerase II: candidate for a Tat cofactor. *J Virol, 69*, 1612-20. ↗

Hyperphosphorylation (Ser2) of RNA Pol II CTD by the P-TEFb(Cyclin T1:Cdk9) complex ↗

Location: Formation of HIV-1 elongation complex containing HIV-1 Tat

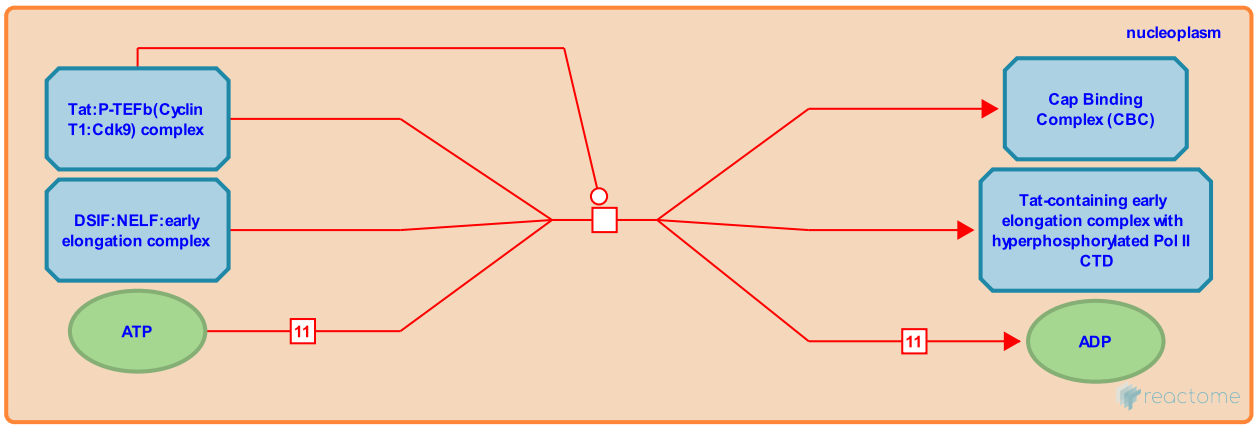
Stable identifier: R-HSA-167191

Type: transition

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Hyperphosphorylation (Ser2) of RNA Pol II CTD by P-TEFb complex (Homo sapiens)



The association between Tat, TAR and P-TEFb is believed to bring the catalytic subunit of P-TEFb(Cyclin T1:Cdk9) in close proximity to Pol II where it hyperphosphorylates the CTD of Pol II (Herrmann et al., 1995; Zhou et al. 2000). In the presence of Tat, P-TEFb(Cyclin T1:CDK9) has been shown to phosphorylate serine 5 in addition to serine 2 suggesting that modification of the substrate specificity of CDK9 may play a role in the ability of Tat to promote transcriptional elongation (Zhou et al. 2000).

Literature references

Kashanchi, F., Brady, JN., Halanski, MA., Radonovich, MF., Price, DH., Zhou, M. et al. (2000). Tat modifies the activity of CDK9 to phosphorylate serine 5 of the RNA polymerase II carboxyl-terminal domain during human immunodeficiency virus type 1 transcription. *Mol Cell Biol, 20*, 5077-86. ↗

Rice, AP., Herrmann, CH. (1995). Lentivirus Tat proteins specifically associate with a cellular protein kinase, TAK, that hyperphosphorylates the carboxyl-terminal domain of the large subunit of RNA polymerase II: candidate for a Tat cofactor. *J Virol, 69*, 1612-20. ↗

Editions

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Phosphorylation of NEFL by the P-TEFb(Cyclin T1:Cdk9) complex ↗

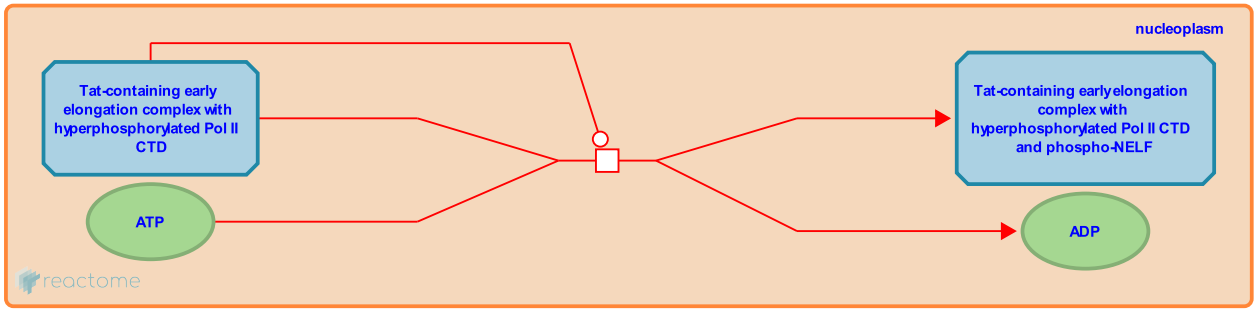
Location: Formation of HIV-1 elongation complex containing HIV-1 Tat

Stable identifier: R-HSA-170706

Type: transition

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease



Phosphorylation of the RD subunit of NEFL by P-TEFb(Cyclin T1:Cdk9) results in the dissociation of NEFL from TAR as well as the conversion of NEFL to an elongation factor (Fujinaga et al., 2004)

Followed by: Phosphorylation of DSIF by the P-TEFb(Cyclin T1:Cdk9) complex

Literature references

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. ↗

Editions

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Phosphorylation of DSIF by the P-TEFb(Cyclin T1:Cdk9) complex ↗

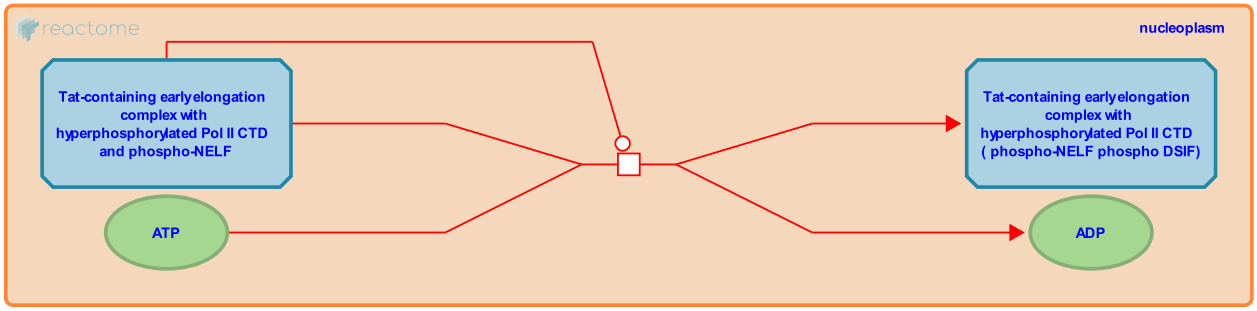
Location: Formation of HIV-1 elongation complex containing HIV-1 Tat

Stable identifier: R-HSA-170704

Type: transition

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease



Phosphorylation of the Spt5 subunit of DSIF by P-TEFb(Cyclin T1:Cdk9) results in the conversion of DSIF to an elongation factor (Ivanov al. 2000).

Preceded by: Phosphorylation of NEFL by the P-TEFb(Cyclin T1:Cdk9) complex

Followed by: Recruitment of elongation factors to form HIV-1 elongation complex

Literature references

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. ↗

Editions

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2006-01-11	Edited	Matthews, L.

Recruitment of elongation factors to form HIV-1 elongation complex ↗

Location: Formation of HIV-1 elongation complex containing HIV-1 Tat

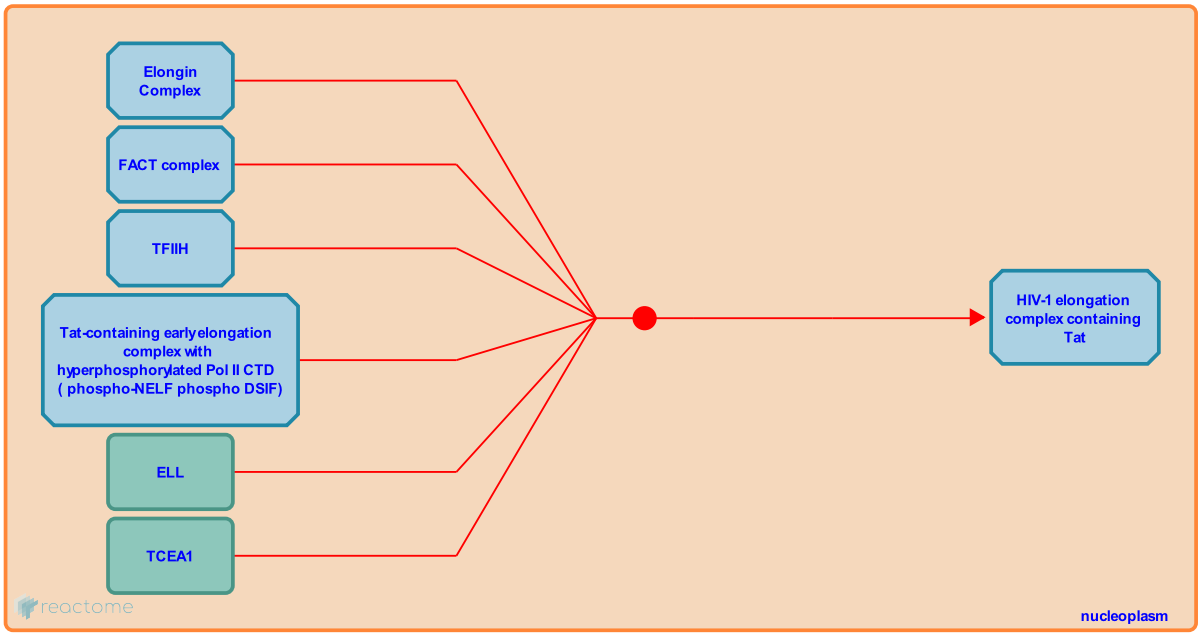
Stable identifier: R-HSA-167196

Type: binding

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Recruitment of elongation factors to form elongation complex (Homo sapiens)



At the beginning of this reaction, 1 molecule of 'FACT complex', 1 molecule of 'Elongin Complex', 1 molecule of 'TFIIH', 1 molecule of 'RNA polymerase II elongation factor ELL', 1 molecule of 'Tat-containing early elongation complex with hyperphosphorylated Pol II CTD (phospho-NELF phospho DSIF)', and 1 molecule of 'TFIIS protein' are present. At the end of this reaction, 1 molecule of 'HIV-1 elongation complex containing Tat' is present.

This reaction takes place in the 'nucleus'.

Preceded by: Phosphorylation of DSIF by the P-TEFb(Cyclin T1:Cdk9) complex

Literature references

Conaway, JW., Shilatifard, A., Conaway, RC. (2003). The RNA polymerase II elongation complex. *Annu Rev Biochem, 72*, 693-715. ↗

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