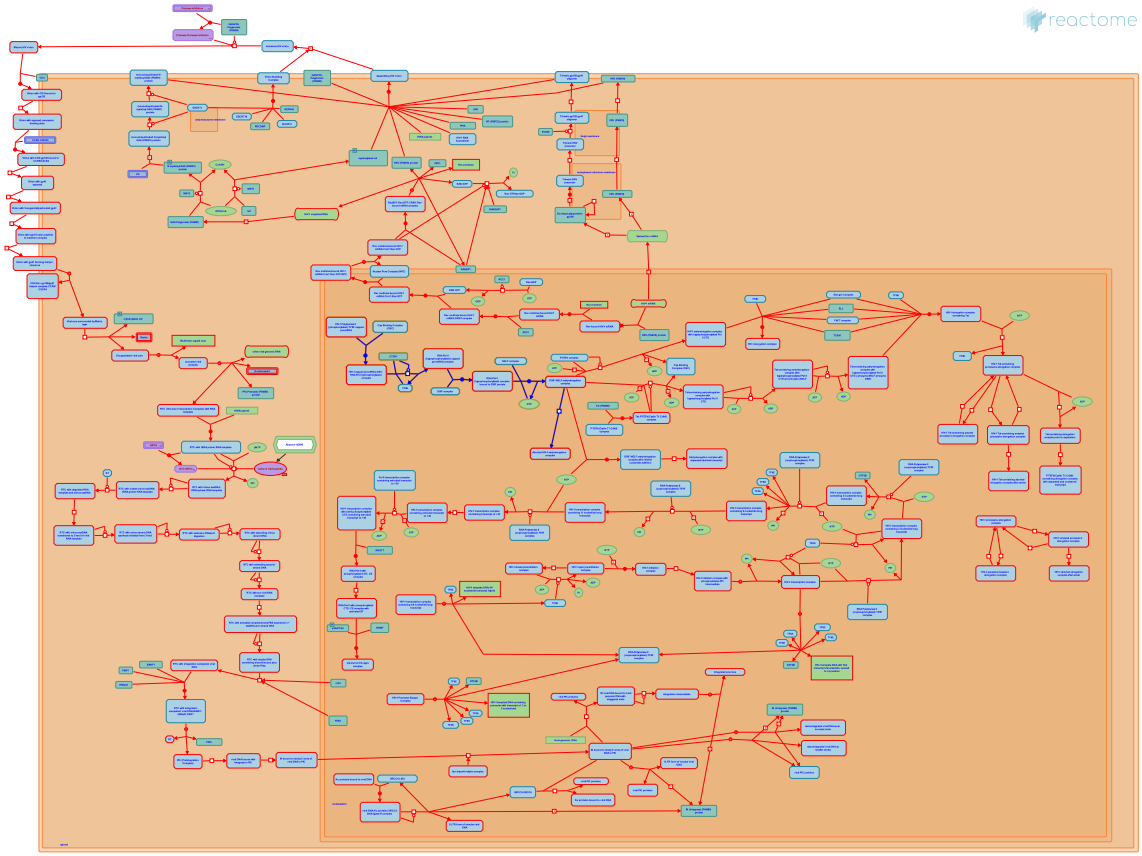
Formation of the HIV-1 Early Elongation Complex



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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. ↗

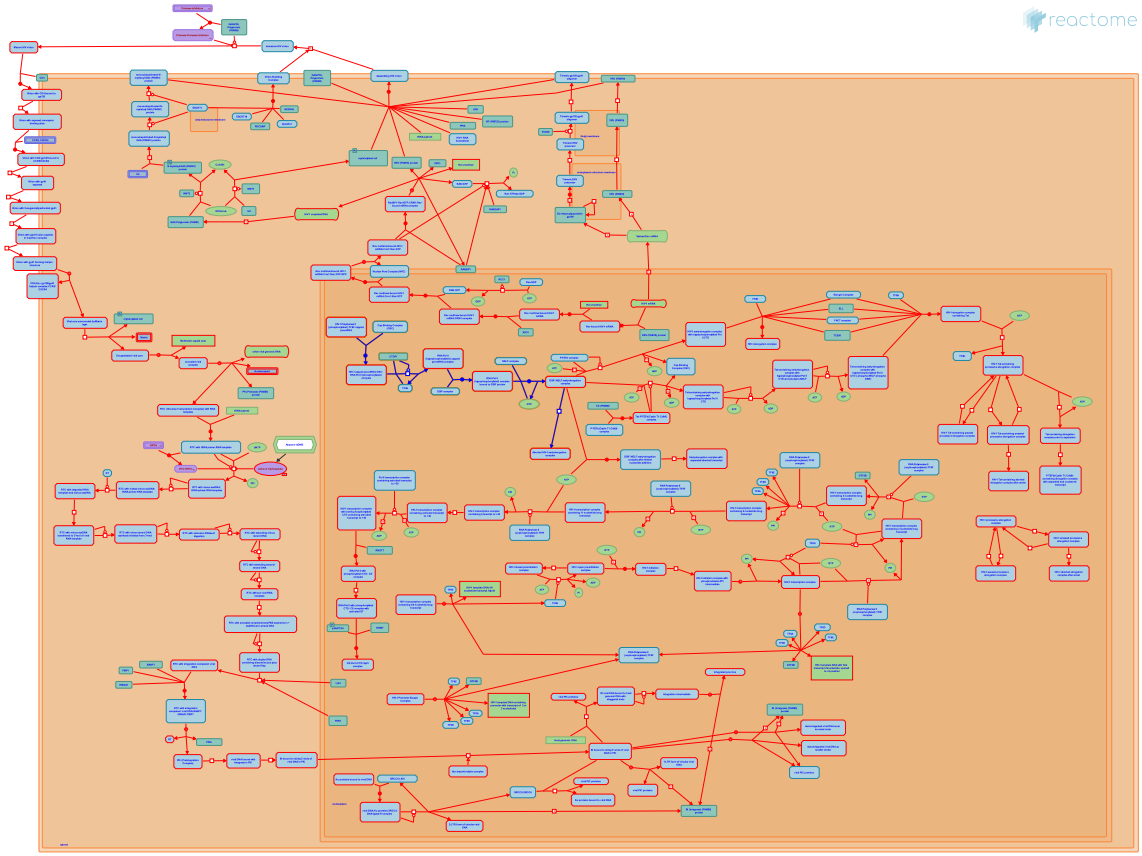
Formation of the HIV-1 Early Elongation Complex ↗

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

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Hypophosphorylation of RNA Pol II CTD by FCP1P protein ↗

Location: Formation of the HIV-1 Early Elongation Complex

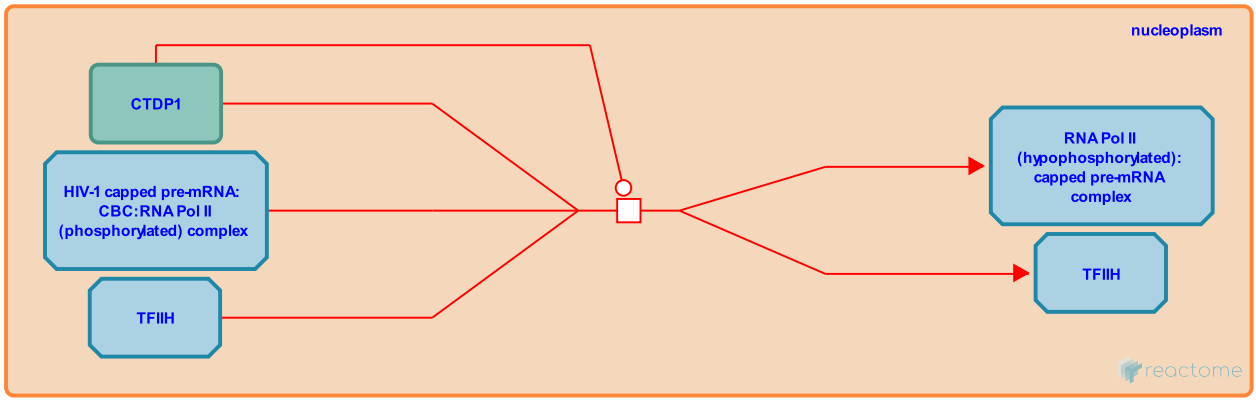
Stable identifier: R-HSA-167072

Type: transition

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Hypophosphorylation of RNA Pol II CTD by FCP1P protein (Homo sapiens)



This HIV-1 event was inferred from the corresponding human RNA Pol II transcription event. FCP1 dephosphorylates RNAP II in ternary elongation complexes as well as in solution and, therefore, is thought to function in the recycling of RNAP II during the transcription cycle. Biochemical experiments suggest that human FCP1 targets CTDs that are phosphorylated at serine 2 (CTD-serine 2) and/or CTD-serine 5. It is also observed to stimulate elongation independent of its catalytic activity. Dephosphorylation of Ser2 - phosphorylated Pol II results in hypophosphorylated form that disengages capping enzymes (CE).

Preceded by: Recognition and binding of the HIV-1 mRNA cap by the cap-binding complex

Followed by: DSIF complex binds to RNA Pol II (hypophosphorylated)

Literature references

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. ↗

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DSIF complex binds to RNA Pol II (hypophosphorylated) ↗

Location: Formation of the HIV-1 Early Elongation Complex

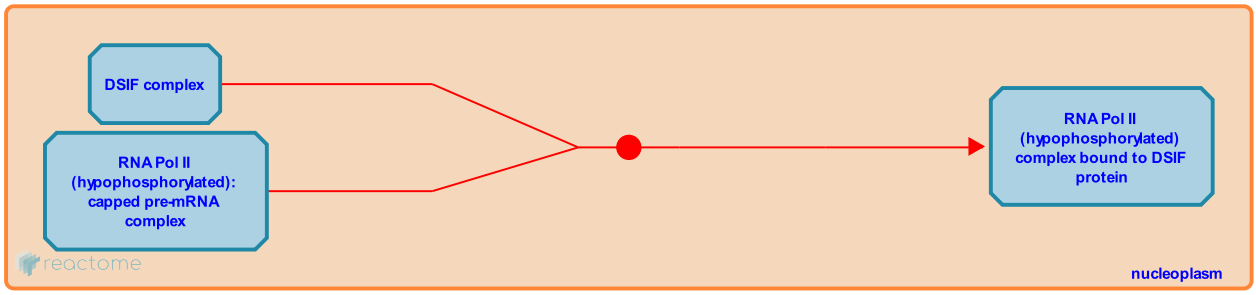
Stable identifier: R-HSA-167083

Type: binding

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: DSIF complex binds to RNA Pol II (hypophosphorylated) (Homo sapiens)



This HIV-1 event was inferred from the corresponding human RNA Pol II transcription event. DSIF is a heterodimer consisting of hSPT4 (human homolog of yeast Spt4- p14) and hSPT5 (human homolog of yeast Spt5-p160) (Wada et al. 1998). DSIF association with Pol II may be enabled by Spt5 binding to Pol II creating a scaffold for NELF binding. Spt5 subunit of DSIF can be phosphorylated by P-TEFb (Ivanov et al. 2000).

Preceded by: Hypophosphorylation of RNA Pol II CTD by FCP1P protein

Followed by: Formation of DSIF:NELF:HIV-1 early 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. ↗

Takagi, T., Wada, T., Handa, H., Watanabe, D., Yamaguchi, Y. (1999). Evidence that P-TEFb alleviates the negative effect of DSIF on RNA polymerase II-dependent transcription in vitro. *EMBO J, 17*, 7395-403. ↗

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. ↗

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. ↗

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Formation of DSIF:NELF:HIV-1 early elongation complex ↗

Location: Formation of the HIV-1 Early Elongation Complex

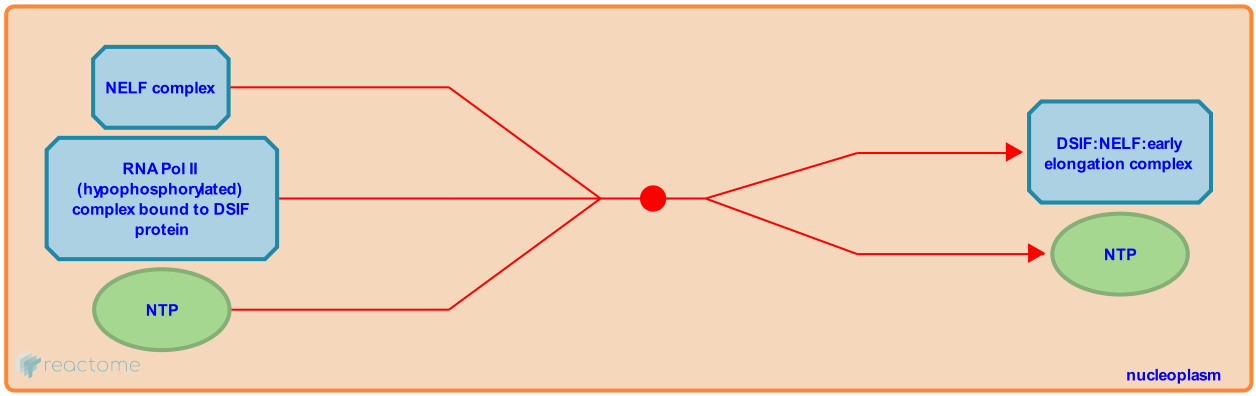
Stable identifier: R-HSA-167085

Type: binding

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Formation of DSIF:NELF:early elongation complex (Homo sapiens)



This HIV-1 event was inferred from the corresponding human RNA Pol II transcription event. NELF complex is a ~ 300 kDa multiprotein complex composed of 5 peptides (A - E): ~66,61,59,58 and 46 kDa (Yamaguchi et al 1999). All these peptides are required for NELF-mediated inhibition of Pol II elongation. NELF complex has been reported to bind to the pre-formed DSIF:RNA Pol II complex that may act as a scaffold for its binding. NELF-A is suspected to be involved in Wolf-Hirschhorn syndrome. Binding of DSIF:NELF to RNA Pol II CTD results in abortive termination of early elongation steps by the growing transcripts.

Preceded by: DSIF complex binds to RNA Pol II (hypophosphorylated)

Followed by: Abortive termination of HIV-1 early transcription elongation by DSIF:NELF

Literature references

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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Abortive termination of HIV-1 early transcription elongation by DSIF:NELF ↗

Location: Formation of the HIV-1 Early Elongation Complex

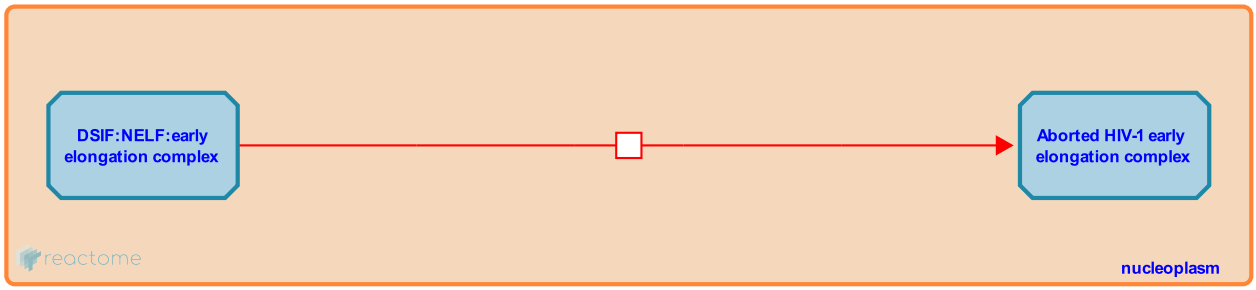
Stable identifier: R-HSA-167478

Type: transition

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Abortive termination of early transcription elongation by DSIF:NELF (Homo sapiens)



In the early elongation phase, shorter transcripts typically of ~30 nt in length are generated due to random termination of elongating nascent transcripts. This abortive cessation of elongation has been observed mainly in the presence of DSIF-NELF bound to Pol II complex. (Reviewed in Conaway et al.,2000; Shilatifard et al., 2003).

Preceded by: Formation of DSIF:NELF:HIV-1 early elongation complex

Literature references

Shilatifard, A., Conaway, JW., Dvir, A., Conaway, RC. (2000). Control of elongation by RNA polymerase II. *Trends Biochem Sci, 25*, 375-80. ↗

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

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Recognition and binding of the HIV-1 mRNA cap by the cap-binding complex ↗

Location: Formation of the HIV-1 Early Elongation Complex

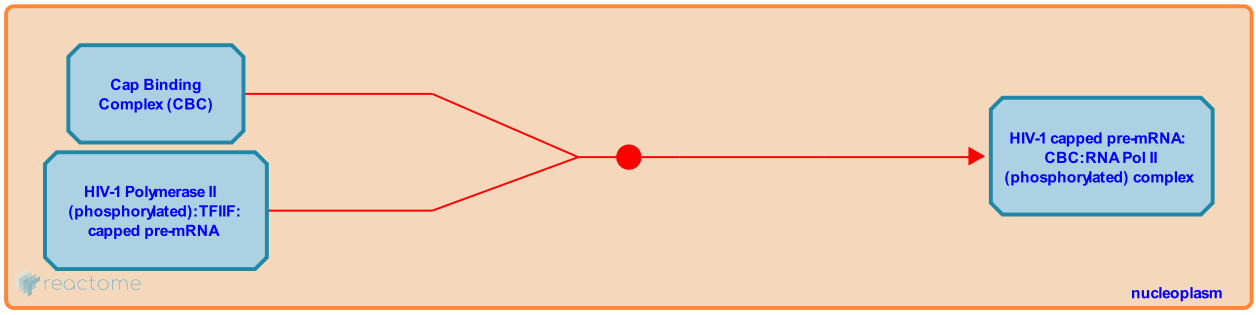
Stable identifier: R-HSA-167089

Type: binding

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease

Inferred from: Recognition and binding of the mRNA cap by the cap-binding complex (Homo sapiens)



The cap binding complex binds to the methylated GMP cap on the nascent mRNA transcript (Gonatopoulos-Pournatzis & Cowling 2014).

Followed by: Hypophosphorylation of RNA Pol II CTD by FCP1P protein

Literature references

Gonatopoulos-Pournatzis, T., Cowling, VH. (2014). Cap-binding complex (CBC). *Biochem. J., 457*, 231-42. ↗

Editions

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