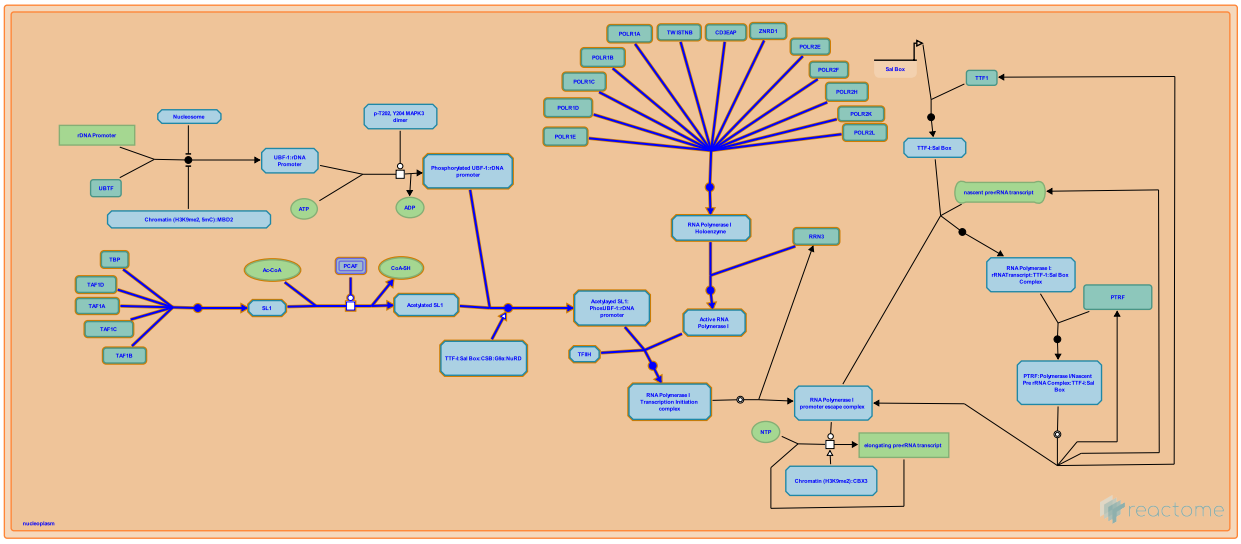
RNA Polymerase I Transcription Initiation



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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.

05/05/2024

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. ↗

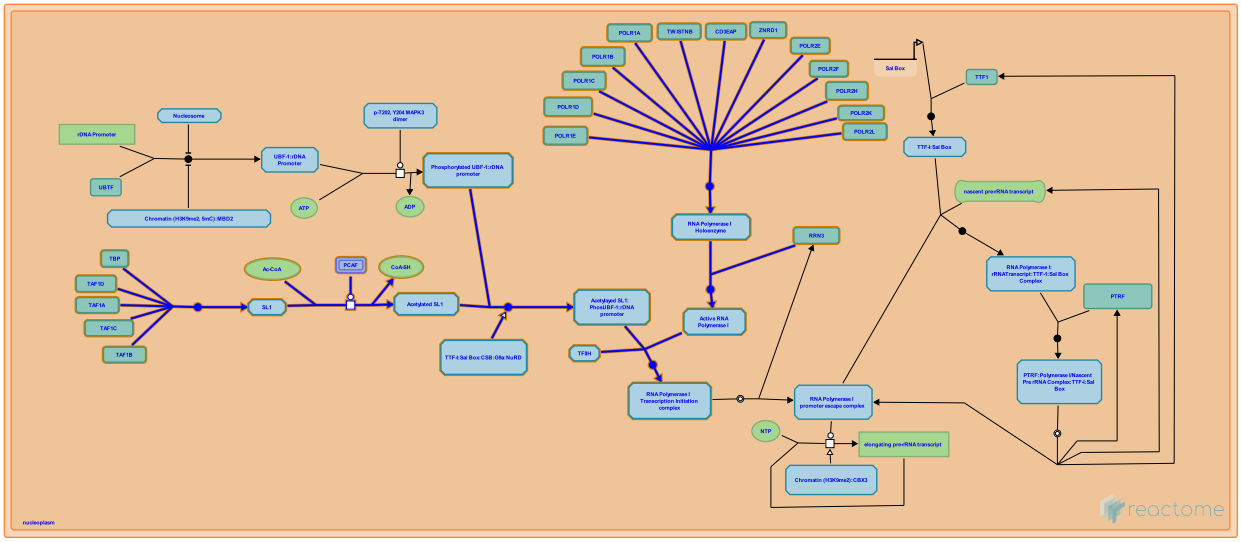
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

RNA Polymerase I Transcription Initiation ↗

Stable identifier: R-HSA-73762

Compartments: nucleolus



During initiation the double-stranded DNA must be melted and transcription begins. SL1 forms and interacts with UBF-1 and the rDNA promoter. It is this platform that will recruit active RNA polymerase I to the SL1:phosphorlated UBF-1:rDNA promoter complex.

Mammalian rRNA genes are preceded by a terminator element that is recognized by the SL1 complex. This SL1 modulated acetylation of the basal Pol I transcription machinery has functional consequences suggesting that the reversible acetylation may be one way to regulate rDNA transcription.

Editions

2003-07-03	Authored	Comai, L.
2024-03-06	Edited	Gillespie, ME.

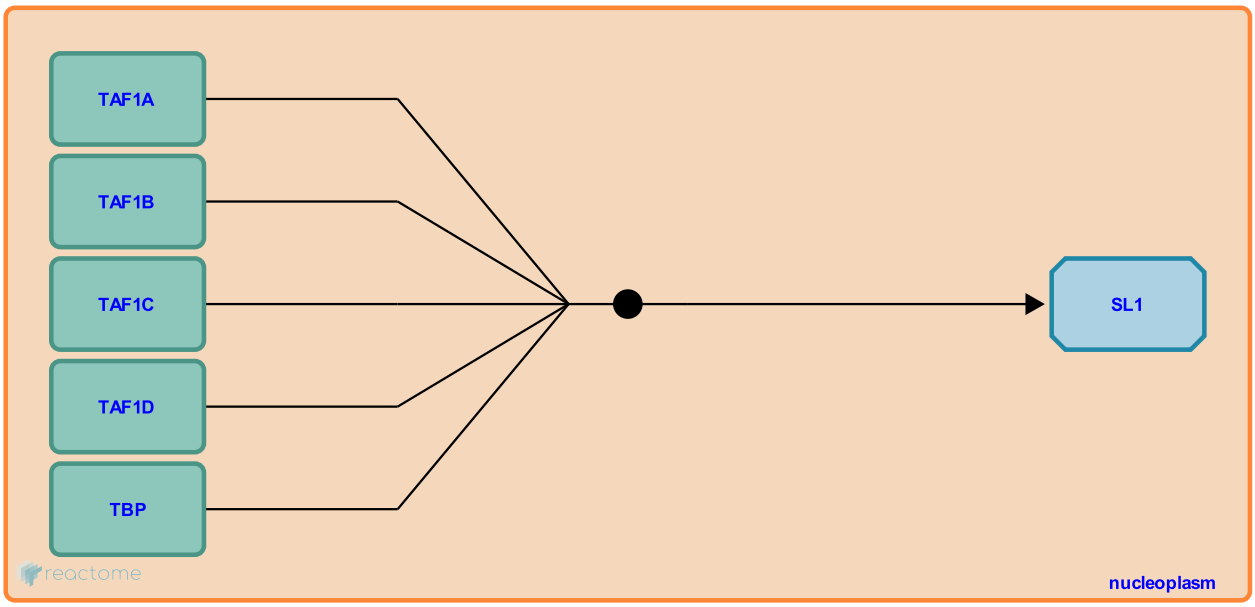
Formation of SL1 ↗

Location: RNA Polymerase I Transcription Initiation

Stable identifier: R-HSA-73729

Type: binding

Compartments: nucleoplasm



Human SL1 is a four subunit complex composed of the TATA-binding protein (TBP) and three TBP-associated factors (TAFs): TAF(1)110, TAF(1)63, and TAF(1)48. Note that none of these three TAFs for Pol I show any homology to the Pol II or Pol III TAFs. TAFs SL1 is a species specific factor.

Followed by: Acetylation of SL1

Literature references

Zhou, S., Beckmann, H., Tjian, R., Zomerdijk, JC., Comai, L. (1995). Reconstitution of transcription factor SL1: exclusive binding of TBP by SL1 or TFIID subunits. *Science, 266*, 1966-72. ↗

Bell, SP., Tjian, R., Pikaard, CS., Reeder, RH. (1989). Molecular mechanisms governing species-specific transcription of ribosomal RNA. *Cell, 59*, 489-97. ↗

Panova, T., Zomerdijk, JC., Panov, K., Gorski, JJ., Pathak, S., Kasciukovic, T. et al. (2007). A novel TBP-associated factor of SL1 functions in RNA polymerase I transcription. *EMBO J., 26*, 1560-8. ↗

Tjian, R., Comai, L., Tanese, N. (1992). The TATA-binding protein and associated factors are integral components of the RNA polymerase I transcription factor, SL1. *Cell, 68*, 965-76. ↗

Acetylation of SL1 ↗

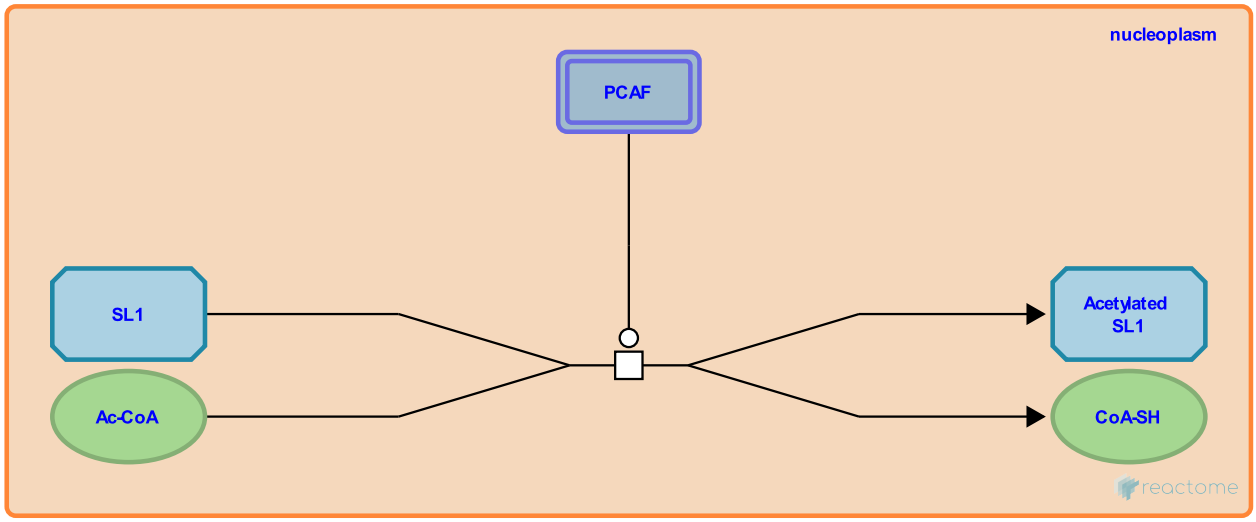
Location: RNA Polymerase I Transcription Initiation

Stable identifier: R-HSA-73736

Type: transition

Compartments: nucleoplasm

Inferred from: Kat2b (Pcaf) acetylates Taf1b in SL1 Complex (Mus musculus)



Acetylation of the TAFI63 subunit of SL1 by PCAF stimulates the association of TAFI63 with DNA and stimulates pol I transcription in vitro. Conversely, deacetylation by the NAD+-dependent deacetylase Sir2 represses pol I transcription.

Preceded by: Formation of SL1

Followed by: Recruitment of Acetylated SL1 to phosUBF-1:rDNA Promoter

Literature references

Nadaud, S., Voit, R., Grummt, I., Muth, V. (2001). Acetylation of TAF(I)68, a subunit of TIF-IB/SL1, activates RNA polymerase I transcription. *EMBO J, 20*, 1353-62. ↗

Editions

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2024-03-06	Edited	Gillespie, ME.

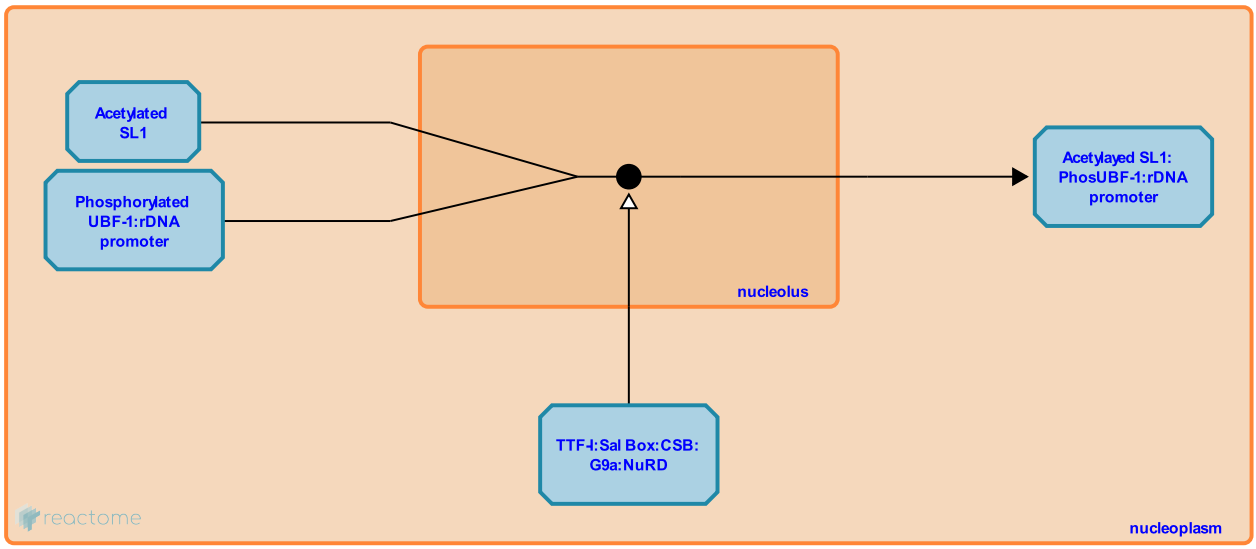
Recruitment of Acetylated SL1 to phosUBF-1:rDNA Promoter ↗

Location: RNA Polymerase I Transcription Initiation

Stable identifier: R-HSA-73739

Type: binding

Compartments: nucleolus



Knockdown of CSB reduces recruitment of SL1 and RNA Polymerase I to active rRNA genes.
Human SL1 does not bind to DNA itself, rather it is recruited to the rDNA promoter through a physical interaction with UBF-1. Phosphorylation of UBF-1 within the carboxy-terminal region is required for SL1 binding. SL1 consists of TATA-binding protein (TBP) and three associated factors (TAFIs). SL1 has no sequence-specific DNA binding activity its recruitment to the promoter being mediated by specific interactions with UBF. Once bound the SL1 complex makes direct contact with the DNA promoter and guides promoter-specific initiation.

Studies to identify the mechanistic relationship between SL1 and UBF-1 have indicated that the interaction between UBF-1 and SL1 is regulated by tumor suppressor proteins such as Rb and P53, although it has also been proposed that Rb prevents UBF-1 from binding to DNA itself.

Preceded by: Acetylation of SL1

Followed by: Recruitment of Active RNA Polymerase I to SL1:phos.UBF-1:rDNA Promoter

Literature references

Beckmann, H., Tjian, R., O'Brien, T., Chen, JL. (1996). Coactivator and promoter-selective properties of RNA polymerase I TAFs. *Science, 270*, 1506-9. ↗

Tuan, JC., Comai, L., Zhai, W. (1999). Recruitment of TATA-binding protein-TAFI complex SL1 to the human ribosomal DNA promoter is mediated by the carboxy-terminal activation domain of upstream binding factor (UBF) and is regulated by UBF phosphorylation. *Mol Cell Biol, 19*, 2872-9. ↗

Comai, L., Zhai, W. (2000). Repression of RNA polymerase I transcription by the tumor suppressor p53. *Mol Cell Biol, 20*, 5930-8. ↗

Editions

2003-07-03	Authored	Comai, L.
2024-03-06	Edited	Gillespie, ME.

Assembly of RNA Polymerase I Holoenzyme (human) ↗

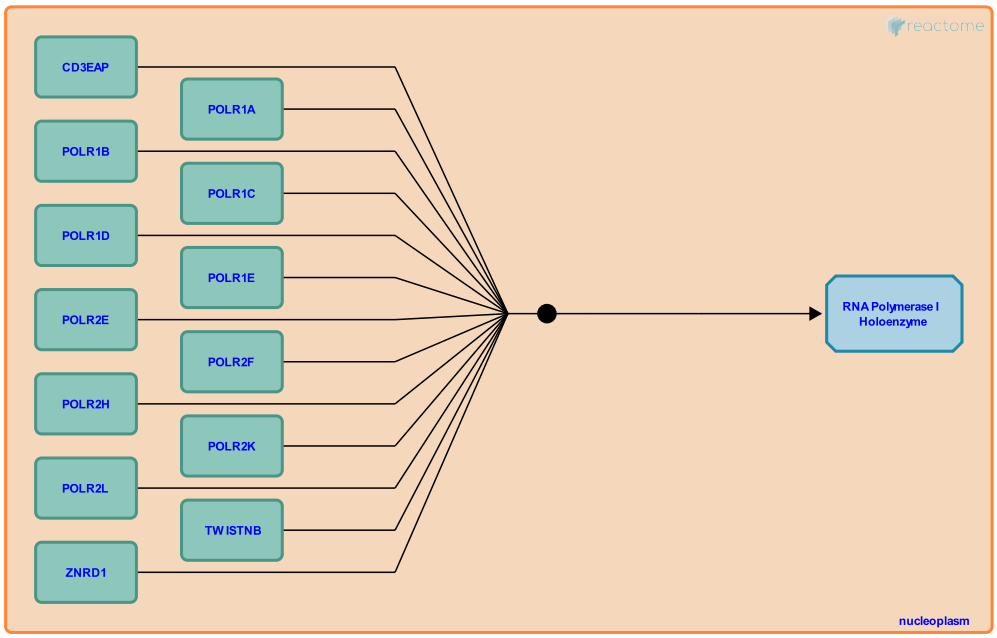
Location: RNA Polymerase I Transcription Initiation

Stable identifier: R-HSA-73865

Type: binding

Compartments: nucleoplasm

Inferred from: Assembly of RNA Polymerase I Holoenzyme (mouse) (Mus musculus)



At the beginning of this reaction, 1 molecule of each of POLR1A (RPA190, A194), POLR1B (RPA135), POLR1C (RPA40), POLR1D (RPA19), POLR1E (PAF53, RPA49), POLR2E (RPB5), POLR2F (RPB6), POLR2H (RPB8), POLR2K (RPABC4, RPB12), POLR2L (RPB10), TWISTNB (RPA43), CD3EAP (CAST, PAF49), and ZNRD1 (RPA12) are present. At the end of this reaction, 1 molecule of 'RNA Polymerase I Holoenzyme (Human)' is present. This reaction takes place in the 'nucleolus'.

Followed by: Binding of RRN3 to RNA Polymerase I

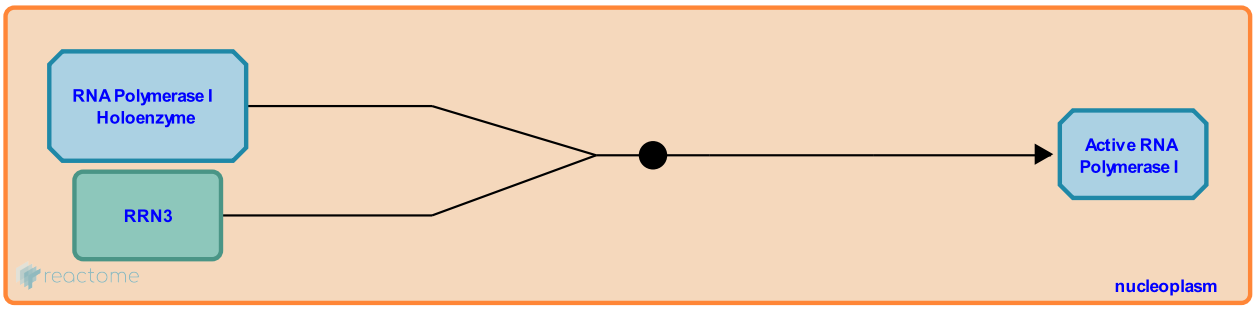
Binding of RRN3 to RNA Polymerase I ↗

Location: RNA Polymerase I Transcription Initiation

Stable identifier: R-HSA-73757

Type: binding

Compartments: nucleoplasm



After the assembly of the RNA Polymerase I Holoenzyme, Rrn3 binding occurs (Engel et al. 2016, Pilsl et al. 2016).

Preceded by: Assembly of RNA Polymerase I Holoenzyme (human)

Followed by: Recruitment of Active RNA Polymerase I to SL1:phos.UBF-1:rDNA Promoter

Literature references

Tschochner, H., Krupp, F., Schultz, P., Milkereit, P., Crucifix, C., Griesenbeck, J. et al. (2016). Structure of the initiation-competent RNA polymerase I and its implication for transcription. *Nat Commun, 7*, 12126. ↗

Plitzko, J., Cramer, P., Engel, C. (2016). RNA polymerase I-Rrn3 complex at 4.8 Å resolution. *Nat Commun, 7*, 12129. ↗

Editions

2003-09-02	Authored	Gillespie, ME.
2024-03-06	Edited	Gillespie, ME.

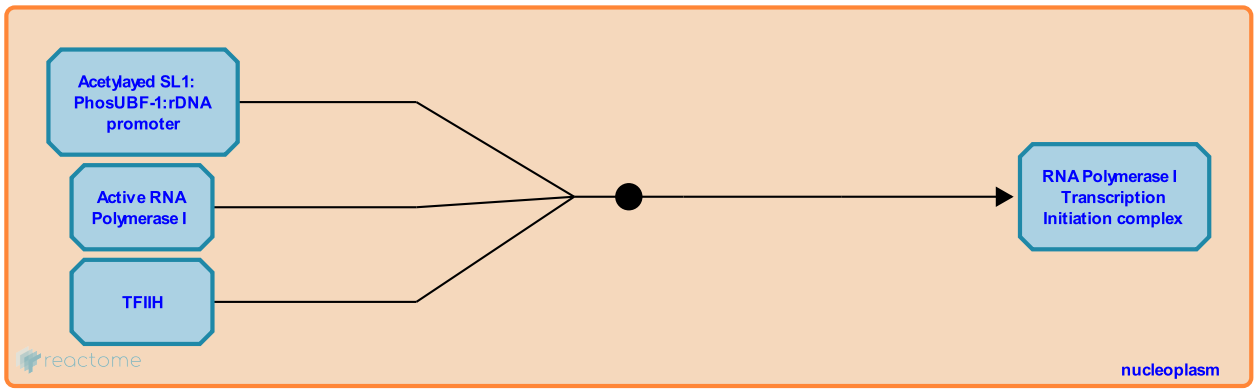
Recruitment of Active RNA Polymerase I to SL1:phos.UBF-1:rDNA Promoter ↗

Location: RNA Polymerase I Transcription Initiation

Stable identifier: R-HSA-73758

Type: binding

Compartments: nucleoplasm



Composed of Acetylated SL1, phosphorylated UBF-1 bound the rDNA promoter as well as the active RNA polymerase holoenzyme, rrn3 and TFIIH the transcription initiation complex is complete. The assembly picture is incomplete, as the point at which TFIIH joins the complex is unknown, though by the time that this complex is formed TFIIH is present (it has been included at this step for completeness). This forms the transcriptionally active enzyme, that is capable of initiating transcription from the rDNA promoter.

Preceded by: Binding of RRN3 to RNA Polymerase I, Recruitment of Acetylated SL1 to phosUBF-1:rDNA Promoter

Literature references

Zentgraf, H., Grummt, I., Hoffmann-Rohrer, U., Zhao, J., Yuan, X. (2002). Multiple interactions between RNA polymerase I, TIF-IA and TAF(I) subunits regulate preinitiation complex assembly at the ribosomal gene promoter. *EMBO Rep, 3*, 1082-7. ↗

Editions

2003-07-03	Authored	Comai, L.
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