RNA polymerase II transcribes snRNA genes

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12/11/2022
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.

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Literature references


Reactome database release: 82

This document contains 1 pathway and 11 reactions (see Table of Contents)
Small nuclear RNAs (snRNAs) play key roles in splicing and some of them, specifically the U1 and U2 snRNAs, are encoded by multicopy snRNA gene clusters containing tandem arrays of genes, about 30 in the RNU1 cluster (Bernstein et al. 1985) and about 10-20 in the RNU2 cluster (Van Ardsell and Weiner 1984). Whereas U6 snRNA genes are transcribed by RNA polymerase III, U1, U2, U4, U4atac, U5, U11, and U12 genes are transcribed by RNA polymerase II. Transcription of the U1 and U2 genes has been most extensively studied and the other snRNA genes as well as other genes with similar promoter structures, for example the SNORD13 gene, are inferred to be transcribed by similar reactions. The snRNA genes transcribed by RNA polymerase II are distinguished from mRNA-encoding genes by the presence of a proximal sequence element (PSE) rather than a TATA box and the presence of the Integrator complex rather than the Mediator complex (reviewed in Egloff et al. 2008, Jawdeker and Henry 2008).

The snRNA genes are among the most rapidly transcribed genes in the genome. The 5' transcribed region of the U2 snRNA gene is largely single-stranded during interphase and metaphase (Pavelitz et al. 2008) and chromatin within the transcribed region is cleared of nucleosomes (O'Reilly et al. 2014). Transcriptional activation of the RNA polymerase II transcribed snRNA genes begins with binding of transcription factors to the distal sequence element (DSE) of the promoter (reviewed in Hernandez 2001, Egloff et al. 2008, Jawdeker and Henry 2008). The factors, which include POU2F1 (Oct-1), POU2F2 (Oct-2), ZNF143 (Staf) and Sp1, promote binding of the SNAPc complex (also known as PTF and PBP) to the PSE. SNAPc helps clear the gene of nucleosomes (O'Reilly et al. 2014) and recruits initiation factors (TFIIA, TFIIB, TFIIE, TFIIF, and snTAFc:TBP) which recruit RNA polymerase II. Phosphorylation of the C-terminal domain (CTD) of RNA polymerase II (reviewed in Egloff and Murphy 2008) by CDK7 recruits RPAP2 and the Integrator complex, which is required for later processing of the 3' end of the pre-snRNA transcript (reviewed in Chen and Wagner 2010, Baillat and Wagner 2015). The Little Elongation Complex (LEC) also ap-
pears to bind around the time of transcription initiation (Hu et al. 2013). As transcription proceeds, RPAP2 dephosphorylates serine-5 and P-TEFb phosphorylates serine-2 of the CTD. As transcription reaches the end of the snRNA gene serine-7 of the CTD is phosphorylated. These marks serve to bind protein complexes and are required for 3' processing of the pre-snRNA (reviewed in Egloff and Murphy 2008). After transcription proceeds through the conserved 3' processing sequence of the pre-snRNA the Integrator complex cleaves the pre-snRNA. Transcription then terminates downstream in a less well characterized reaction that requires elements of the polyadenylation system.

**Literature references**


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POU2F1 (OCT1) or POU2F2 (OCT2), SP1, and ZNF143 (STAF) bind the DSE of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

Location: RNA polymerase II transcribes snRNA genes

Stable identifier: R-HSA-6807496

Type: binding

Compartments: nucleoplasm

An octamer binding factor, POU2F1 (Oct-1) or POU2F2 (Oct-2), SP1, ZNF143 (Staf) and possibly other transcription factors bind the distal sequence element (DSE) in the promoter of the snRNA gene (Murphy et al. 1992, Strom et al. 1996, Murphy 1997, Hovde et al. 2002). These upstream transcription factors enhance subsequent binding of the SNAPc complex to the downstream proximal sequence element (PSE) of the promoter.

Followed by: SNAPc binds PSE of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

Literature references


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https://reactome.org
SNAPc binds PSE of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6810239

**Type:** binding

**Compartments:** nucleoplasm


**Preceded by:** POU2F1 (OCT1) or POU2F2 (OCT2), SP1, and ZNF143 (STAF) bind the DSE of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

**Followed by:** General transcription factors bind SNAPc:POU2F1:ZNF143:snRNA gene

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The promoter of an snRNA gene binds the basal transcription factors TFIIA, TFIIIB (GTF2B), TFIIIE, and TFIIIF (Bernues et al. 1993, Kuhlman et al. 1999). Rather than the TFIID complex found at promoters of mRNA-encoding genes, a unique complex containing TBP (Sadowski et al. 1993) and snTAFc is present at promoters of snRNA genes (Zaborowska et al. 2012). The P-TEFb complex is also observed at snRNA genes, however, it seems to play a role more in 3' processing than in elongation (Medlin et al. 2005). CDK7 is also present and phosphorylates the C-terminal domain of RNA polymerase II (Glover-Cutter et al. 2009).

**Preceded by:** SNAPc binds PSE of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

**Followed by:** RNA polymerase II binds initiation factors at promoter of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

**Literature references**


RNA polymerase II binds initiation factors at promoter of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6810238

**Type:** binding

**Compartments:** nucleoplasm

The basal initiation factors TFIIA, TFIIB, TFIIE, TFIIF, and TBP:snTAFc recruit unphosphorylated RNA polymerase II to the promoter of the (U1, U2, U4, U5) snRNA gene (Gunderson et al. 1990, Kuhlman et al. 1999, Zaborowska et al. 2012).

**Preceded by:** General transcription factors bind SNAPc:POU2F1:ZNF143:snRNA gene

**Followed by:** CDK7 phosphorylates serine-5 and serine-7 of heptad repeats in C-terminal domain of RNA polymerase II at snRNA promoter

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https://reactome.org
CDK7 phosphorylates serine-5 and serine-7 of heptad repeats in C-terminal domain of RNA polymerase II at snRNA promoter

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6810233

**Type:** transition

**Compartments:** nucleoplasm

CDK7 phosphorylates serine-5 residues of heptad repeats (consensus YSPTSPS) in the C-terminal domain (CTD) of the large subunit (POLR2A) of RNA polymerase II. Serine-7 residues of the heptad repeats are also phosphorylated at promoters of snRNA genes (Egloff et al. 2007) and CDK7 is required for phosphorylation of serine-7 in vivo (Glover-Cutter et al. 2009). P-TEFb and DNA-PK are able to phosphorylate serine-7 in vitro (Glover-Cutter et al. 2009, Egloff et al. 2010). Impairment of CTD phosphorylation does not appear to affect transcription of snRNA genes but rather impairs 3' processing of the pre-snRNA (Medlin et al. 2003, Jacobs et al. 2004).

**Preceded by:** RNA polymerase II binds initiation factors at promoter of snRNA gene (U1, U2, U4, U4atac, U5, U11, U12)

**Followed by:** RPAP2 binds RNA polymerase II phosphorylated at serine-7 residues of heptad repeats in the C-terminal domain

**Literature references**


Uguen, P., Murphy, S., Bentley, DL., Taylor, A., Medlin, JE. (2003). The C-terminal domain of pol II and a DRB-sensitive kinase are required for 3’ processing of U2 snRNA. *EMBO J.*, 22, 925-34.


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https://reactome.org
RPAP2 binds RNA polymerase II phosphorylated at serine-7 residues of heptad repeats in the C-terminal domain

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6810235

**Type:** binding

**Compartments:** nucleoplasm

The protein phosphatase RPAP2 binds RNA polymerase II phosphorylated at serine-7 of the C-terminal domain (CTD) (Egloff et al. 2012). RPRD1A and RPRD1B bind RNA polymerase II with RPAP2 and appear to act as scaffolds for the complex (Ni et al. 2011, Ni et al. 2014).

**Preceded by:** CDK7 phosphorylates serine-5 and serine-7 of heptad repeats in C-terminal domain of RNA polymerase II at snRNA promoter

**Followed by:** Pre-snRNA transcript initiation, Integrator binding, LEC binding

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Pre-sRNA transcript initiation, Integrator binding, LEC binding

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6814549

**Type:** omitted

**Compartments:** nucleoplasm

In an unknown order of events, RNA polymerase II initiates transcription and the Integrator complex (Baillat et al. 2005) and Little Elongation Complex (LEC, Hu et al. 2013) are recruited to phosphorylated RNA polymerase II (Egloff et al. 2010). The Integrator complex interacts with RPAP2, which binds phosphoserine-7 of the C-terminal domain (CTD) of RNA polymerase II and is required for recruitment of Integrator (Egloff et al. 2007, Egloff et al. 2012). RPAP2 interacts with the putative scaffold proteins RPRD1A and RPRD1B at the CTD (Ni et al. 2011, Ni et al. 2014) and DSIF is required for recruitment of Integrator (Skaar et al. 2015). The Integrator complex does not seem to play a significant role in subsequent elongation of the pre-sRNA transcript but is critical for processing of the 3' end of the pre-sRNA.

**Preceded by:** RPAP2 binds RNA polymerase II phosphorylated at serine-7 residues of heptad repeats in the C-terminal domain

**Followed by:** Pre-sRNA is elongated and capped with 7-methylguanosine

**Literature references**


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Pre-snRNA is elongated and capped with 7-methylguanosine

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6814559

**Type:** omitted

**Compartments:** nucleoplasm

A 7-methylguanosine triphosphate group is added to the 5' end of the pre-snRNA during transcription elongation (Mattaj 1986). The capping enzyme and cap methyltransferase involved in mRNA capping may also be responsible for this reaction. In the case of mRNA capping, the capping enzyme is targeted to the pre-mRNA by interaction with the phosphorylated C-terminal domain (CTD) of RNA polymerase II (McCracken et al. 1997). During elongation, the phosphorylation pattern of the CTD also changes: serine-5 is dephosphorylated by RPAP2 (Egloff et al. 2012) interacting with RPRD1A and RPRD1B (Ni et al. 2011, Ni et al. 2014) and serine-2 is phosphorylated by P-TEFb. Serine-7 is also phosphorylated, possibly, however the responsible kinase is not certain. The order of the capping and phosphorylation events is unknown.

**Preceded by:** Pre-snRNA transcript initiation, Integrator binding, LEC binding

**Followed by:** CBCAP complex binds 7-methylguanosine cap of snRNA

**Literature references**

Siderovski, D., Hessel, A., Fong, N., Bentley, DL., Foster, S., Yankulov, K. et al. (1997). 5'-Capping enzymes are targeted to pre-mRNA by binding to the phosphorylated carboxy-terminal domain of RNA polymerase II. *Genes Dev.*, 11, 3306-18.


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Guo, H., Marcon, E., Young, P., Li, J., Ruan, ED., Olsen, JB. et al. (2011). Control of the RNA polymerase II phosphorylation state in promoter regions by CTD interaction domain-containing proteins RPRD1A and RPRD1B. *Transcription, 2*, 237-42.

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CBCAP complex binds 7-methylguanosine cap of snRNA

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6814885

**Type:** binding

**Compartments:** nucleoplasm

As the capped pre-snRNA continues to be elongated, the CBCAP complex comprising NCBP1 (CBP80), NCBP2 (CBP20), SRRT (ARS2) and PHAX binds the 7-methylguanosine cap (Hallais et al. 2013). The CBCAP complex enhances 3' processing of the pre-snRNA (Hallais et al. 2013) and participates in export of the snRNA from the nucleus to the cytosol, where the snRNA is further modified and assembled with proteins into pre-snRNPs.

**Preceded by:** Pre-snRNA is elongated and capped with 7-methylguanosine

**Followed by:** Integrator complex processes the 3' end of snRNA

**Literature references**


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[https://reactome.org](https://reactome.org)
Integrator complex processes the 3' end of snRNA

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6814555

**Type:** omitted

**Compartments:** nucleoplasm

Transcription of the pre-snRNA extends through a conserved region, the 3' box, and terminates downstream. The heterodimeric subunits INTS9 and INTS11 within the Integrator complex form an endoribonuclease that cleaves the pre-snRNA at a location 5' to the 3' box (Baillat et al. 2005, Abrecht and Wagner 2012, Skaar et al. 2015), releasing the capped snRNA bound to the cap binding complex. Factors that bind the 5' cap of the pre-snRNA enhance processing at the 3' end (Hallais et al. 2013) and polyadenylation factors PCF11 and SKU72 are required for transcription termination (O'Reilly et al. 2014). The remainder of the transcript downstream of the cleavage site is presumably degraded by exoribonuclease.

**Preceded by:** CBCAP complex binds 7-methylguanosine cap of snRNA

**Followed by:** Dephosphorylation and dissociation of RNA polymerase II at 3' end of snRNA gene

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Dephosphorylation and dissociation of RNA polymerase II at 3' end of snRNA gene

**Location:** RNA polymerase II transcribes snRNA genes

**Stable identifier:** R-HSA-6814554

**Type:** omitted

**Compartments:** nucleoplasm

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

Like RNA polymerase II at mRNA-encoding genes, RNA polymerase II at snRNA genes is believed to be dephosphorylated at the C-terminal domain (CTD) in order to begin another round of transcription. RNA polymerase II and factors bound to its C-terminal domain (CTD) dissociate and RNA polymerase II dissociates from the 3' end of the snRNA gene. The order of events is unclear.

**Preceded by:** Integrator complex processes the 3' end of snRNA

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