Nuclear transcription in S. cerevisiae is performed by three multisubunit nuclear RNA polymerasesthat are conserved in all eukaryotes. The roles of these three RNA polymerases are generally conserved across eukaryotes, particularly with respect to production of rRNAs, mRNAs, and tRNAs, though production of other small RNAs is somewhat variable between RNAP II and RNAP III in different species. In S. cerevisiae, RNA polymerase I transcribes rDNA to produce the 35S primary rRNA transcript that is processed to produce three of the four mature ribosomal rRNAs: 25S, 18S, and 5.8S. RNA polymerase II produces all nuclear mRNAs, all of the snoRNAs except snR52, four of the five snRNAs, the RNase MRP RNA encoded by NME1, and the telomerase RNA encoded by TLC1. RNA polymerase III produces the 5S rRNA, all nuclear tRNAs, the U6 snRNA, the snR52 snoRNA, the RNase P RNA encoded by RPR1, and the 7SL RNA component of the signal recognition particle encoded by SCR1.Coordinate regulation of these three RNA polymerases is essential, since in rapidly growing yeast cells, much of the transcriptional output of the cell is devoted to the production of ribosomes. About 60% of total cellular transcription is devoted to transcription by RNAP I of the rRNA genes, which comprise about 10% of the entire genome. While mRNAs generally only comprise 5% of total cellular RNA and the 137 ribosomal proteingenes represent only 2% of the genome, it is estimated that 50% of RNAP II transcription occurs on RP genes. RNAP II is also responsible for production of the majority of the snoRNAs, which are collectively involved in maturation of the ribosome. RNAP III plays a similarly important role in production of ribosomes and the process of translation, producing both the 5S rRNA and all nuclear tRNAs, which constitute about 15% of total cellular RNA. The TOR pathway is a major factor in this coordinate regulation as it regulates the activity of all three nuclear RNAPs in response to nutrient availability and growth conditions.In addition to producing the majority of cellular RNA, RNAP I and RNAP III may also play roles in nuclear architecture and genome organization. RNAP I activity may be involved in organizing the rDNA repeats into the nucleolus. Active tRNA genes transcribed by RNAP III appear to act as chromatin boundary elements that affect both transcription and DNA replication. Additionally, recombination between dispersed tRNA genes may be a source of genetic instability and evolutionary change.Five genesencode subunits common to all three of the nuclear RNA polymerases. Two genesencode subunits present in both RNAP I and RNAP III; RPB3 and RPB11 encode the corresponding RNAP II subunits. Five more subunits are encoded by a separate gene for each polymerase, but are considered functional equivalents of each other. Thus there are twelve subunits that are conserved in all three of the nuclear RNA polymerases, eleven of which correspond to subunits of Archaeal RNAPs, and five of which also correspond to the subunits of E. coli RNAP. In each, ten of these comprise the enzyme cores, while Rpb4/7, Rpa14/43, and Rpc17/25form heterodimers which associate with this core and have roles in initiation. RNAPs I and III also have two subunits which are homologous to the subunits of the TFIIF general initiation factor for RNAP II, and RNAP III has three additional unique subunits. For tables showing the correspondence between the subunits of the three nuclear RNA polymerases in S. cerevisiae see Cramer et al. 2008and Werner et al. 2009; to see the correspondence with those of Archaea and bacteria see Cramer 2002.About RNA polymerase I... In S. cerevisiae, the RNA polymerase I enzyme is composed of fourteen subunits. RPB5, RPO26, RPB8, RPC10, RPB10, RPC40, and RPC19 encode subunits shared with one or both of the other two nuclear RNA polymerases. RPA49 and RPA34 encode subunits with counterparts in RNA polymerase III and RPA190, RPA135, RPA43, RPA14, and RPA12 encode subunits with counterparts in both RNA polymerases II and III.Most of the genes encoding subunits of RNA polymerase I are essentialand elegant genetic experiments have shown that production of the large rRNA transcript is the only essential role of these genes. However, null mutations in any of four of the genesencoding subunits present only in RNAP I produce viable strains. While a triple mutant strain lacking functional RPA49, RPA34, and RPA12 is viable, inactivating any one of these genes in combination with RPA14 is lethal. Thus these four subunits are dispensible individually but collectively become essential. Rpa49p and Rpa34p, as expected from their similarity to TFIIF, contribute to the elongation properties of RNAP I. Rpa12p contains a C-terminal domain with similarity to the RNAP II elongation factor TFIISwhich appears to activate the transcript cleavage activity intrinsic to the RNAP I catalytic core. Mutations in core subunits such as RPA190, RPA135, RPC40, and RPC19 often affect the basic functions of core enzyme assembly and catalytic properties of initiation, elongation, or termination, as well as the association of the core enzyme with the other complexes required for RNAP I function in vivo.RNAP I transcription requires a number of factors in addition to the polymerase itself: TATA-binding protein, the initiation factor Rrn3, the core factor CF, and the upstream activating factor UAF. While some of these factors have mammalian homologs, others are more diverged, as might be expected from the fact that there is little conservation of rDNA promoter sequences across taxonomic groupings although some structural elements are conserved. UAF binds to the promoter and recruits CF and a complex of Rrn3p associated with RNAP I. Rrn3p plays a key role in the regulation of RNAP I activity, as RNAP I is only able to initiate transcription when it is associated with Rrn3p, but any of the RNAP I transcription factors may serve as a target for regulation. In addition, the TFIIH factor, originally characterized as a RNAP II transcription factor, is also required for productive transcriptional elongation by RNAP I and for coupling of DNA repair to rDNA transcription. Numerous regulatory pathways are involved in the complex regulation of RNAP I in response to growth signals, including both the TOR and MAP kinase signaling pathways and chromatin remodeling activities. Thus control of RNAP I activity is central to control of ribosome production and growth control in S. cerevisiae.About RNA polymerase II In S. cerevisiae, the RNA polymerase II core enzymeis composed of twelve subunits. RPO21, RPB2, RPB3, RPB4, RPB7, RPB9, and RPB11 encode subunits unique to RNAP II, while RPB5, RPO26, RPB8, RPC10, and RPB10 encode shared subunits. A subcomplex composed of Rpb4p and Rpb7pis substoichiometric in some growth conditions and easily dissociated during purification. Purified enzyme composed of the remaining 10 subunits is capable of polymerizing RNA in vitro, but does not recognize or initiate at promoter sequences. The structure of the core enzyme has been determined, with and without the Rpb4/7 subcomplex, and provides insight into the specific roles of the subunits within the complex.Most of the genes encoding subunits of RNA polymerase II are essential. However null mutations in rpb4 or rpb9 are not essential in standard laboratory conditions, but become so when cells are subjected to stresses such as reduced or elevated temperature or absence of nutrients such as inositol. While not required for catalytic activity, Rpb4p as part of the Rpb4/7 subcomplex is required for response to heat or cold stress, recovery from stationary phase, and sporulation, and is also thought to be involved in response to transcriptional activators, mRNA export during heat stress, and regulation of transcription coupled repair. Also not required for catalytic activity, Rpb9p is involved in selection of the transcription initiation site and control of fidelity. Partial truncations of the carboxyl terminal domainof the largest subunit RPO21, or conditional mutations in one of the essential subunits, may also produce the combined phenotype of cold sensitivity, heat sensitivity and inositol auxotrophy. This combination of phenotypes appears to be due to sensitivity of specific genes, such as INO1, to reduction in the function or quantity of RNAP II. Mutations in core subunits such as RPO21, RPB2, or RPB3 often affect the basic functions of core enzyme assembly and catalytic properties of initiation, elongation, or termination, as well as the association of the core enzyme with the other complexes required for RNAP II function in vivo.In yeast, as in other eukaryotes, fully competent RNA polymerase II activity in vivo requires the association of the full core enzyme with several other complexes, including the general transcription factorsTFIID, TFIIB, TFIIF, TFIIE, and TFIIH. Some of the GTFs bind directly to DNA to identify the promoter sequence and recruit the remaining GTFs and RNAP II to the promoter to form the preinitiation complex. In addition, Mediator, a large modular complex, is required for RNAP II to respond to gene-specific activators. Some of these factors travel with RNAP II along the transcription unit. When purified together, RNAP II and Mediator are sometimes referred to as \"holoenzyme\", though it appears that multiple \"holoenzymes\" have been purified with slightly varied subunit composition depending on the purification method, which may reflect the modular nature of Mediator as well as the need to respond to different regulatory signals.The largest subunit RPO21 contains a repetitive carboxyl terminal domain, unique to type II RNA polymerases, composed of numerous copies of the seven-amino-acid sequence YSPTSPS. Though the number of repeats varies between the largest subunits of different species, deletion of the entire CTD is invariably lethal even though it is not required in vitro for catalytic activity. The CTD undergoes cycles of phosphorylation and dephosphorylation, especially on serines 2 and 5. Its phosphorylation state regulates interactions of the core enzyme with other protein complexes such as the GTFs, Mediator, and chromatin remodelling enzymes, thus regulating both initiation and elongation in vivo. During production of the primary transcript, the phosphorylation state of the CTD changes to allow the transcribing polymerase to associate with the capping, splicing, polyadenylation, and mRNA export machinery. These associations are required for normal processing of pre-mRNAs to generate mRNAs and to export them to the cytoplasm, as well as for normal termination of transcription by RNAP II. Thus the CTD plays essential roles in the coordinate regulation of gene expression, mRNA production, and the export of mRNAs to the cytoplasm.About RNA polymerase III... In S. cerevisiae, the RNA polymerase III enzyme is composed of seventeen subunits, all of which are essential. RPB5, RPO26, RPB8, RPC10, RPB10, RPC40, and RPC19 encode subunits shared with one or both of the other two nuclear RNA polymerases. RPC53 and RPC37 encode subunits with counterparts in RNAP I, and RPO31, RET1, RPC25, RPC17, and RPC11 encode subunits with counterparts in both RNA polymerases I and II. RPC82, RPC34, and RPC31 encode subunits unique to RNAP III and homologous to a detachable subassembly of human RNAP III implicated in response to specific transcription factors.In contrast to RNAP I and II promoters, most RNAP III promoters are internal to the expressed sequence of the RNA being transcribed, though there are some exceptions such as the well studied U6 snRNA. These internal promoters can be divided into classes based on their organization. Class 1 genes are represented by the 5S rRNA genes, present within the intragenic spacer of the 37S rDNA, and are the only genes which require the specific DNA-binding initiation factor TFIIIA, the archetype zinc finger protein, which then recruits TFIIIC. Class 2 genes comprise the tRNA genes, and others with similar promoter structures, containing internal box A and box B sequence elements which are recognized directly by the six subunit DNA-binding initiation factor TFIIIC. In both classes, TFIIIC recruits TFIIIB, which does not bind to DNA by itself despite the fact that it contains the TATA-binding protein TBP, as well as two other subunits. Once bound to DNA, TFIIIB brings RNAP III to the promoter and helps initiate transcription. RNAP III transcription is regulated by at least two nutrient-sensing signal transduction pathways, RAS and TOR. Both of these work through Maf1p, which is evolutionarily conserved from yeast to humans, and which represses RNAP III activity when yeast cells experience stress or unfavorable growth conditions.