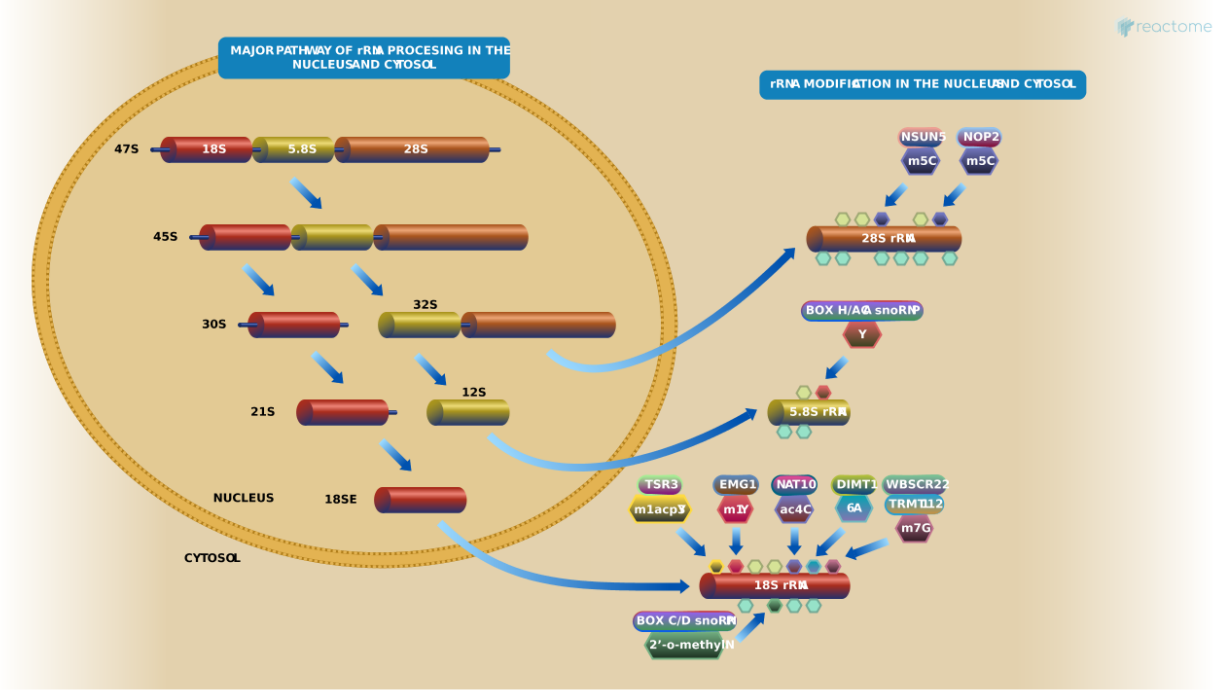
rRNA processing in the nucleus and cytosol



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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.

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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. ↗

rRNA processing in the nucleus and cytosol ↗

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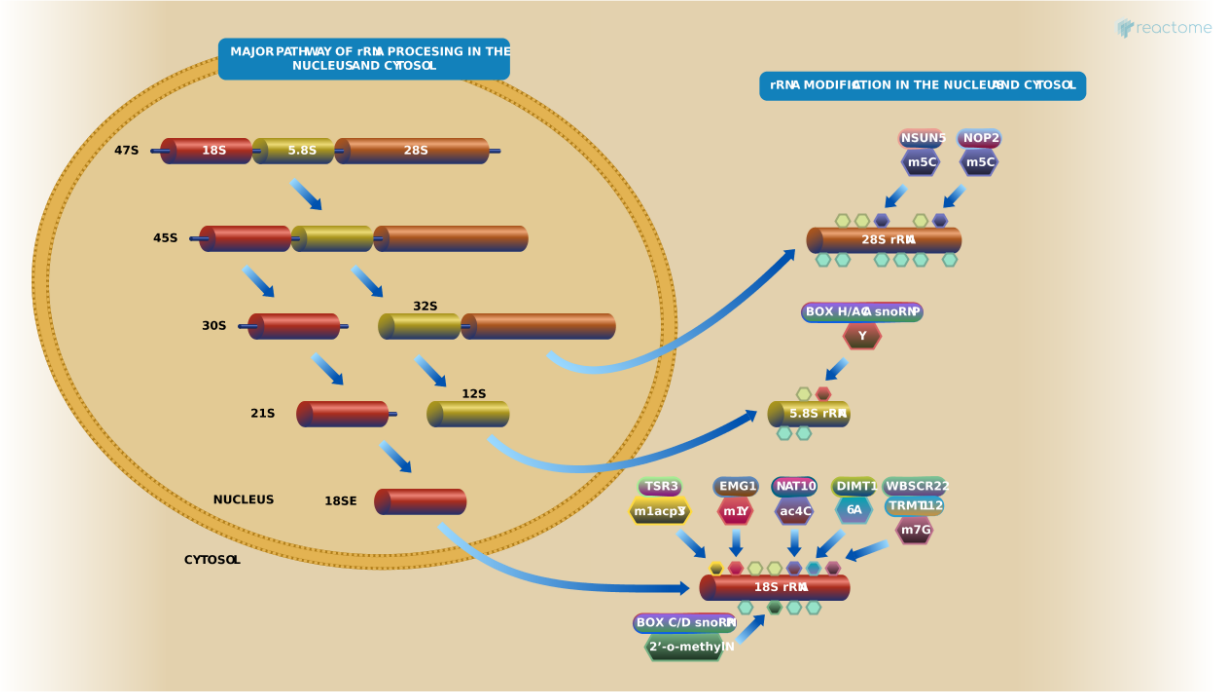

Each eukaryotic cytosolic ribosome contains 4 molecules of RNA: 28S rRNA (25S rRNA in yeast), 5.8S rRNA, and 5S rRNA in the 60S subunit and 18S rRNA in the 40S subunit. The 18S rRNA, 5.8S rRNA, and 28S rRNA are produced by endonucleolytic and exonucleolytic processing of a single 47S precursor (pre-rRNA) (reviewed in Henras et al. 2015). Transcription of ribosomal RNA genes, processing of pre-rRNA, modification of nucleotide residues within the rRNA, and assembly of precursor 60S and 40S subunits occur predominantly in the nucleolus (reviewed in Hernandez-Verdun et al. 2010, Boschi-Muller and Motorin 2013), with a few late reactions occurring in the cytosol.

Literature references

Henras, AK., Plisson-Chastang, C., O'Donohue, MF., Chakraborty, A., Gleizes, PE. (2015). An overview of pre-ribosomal RNA processing in eukaryotes. *Wiley Interdiscip Rev RNA, 6*, 225-42. ↗

Hernandez-Verdun, D., Roussel, P., Thiry, M., Sirri, V., Lafontaine, DL. (2010). The nucleolus: structure/function relationship in RNA metabolism. *Wiley Interdiscip Rev RNA, 1*, 415-31. ↗

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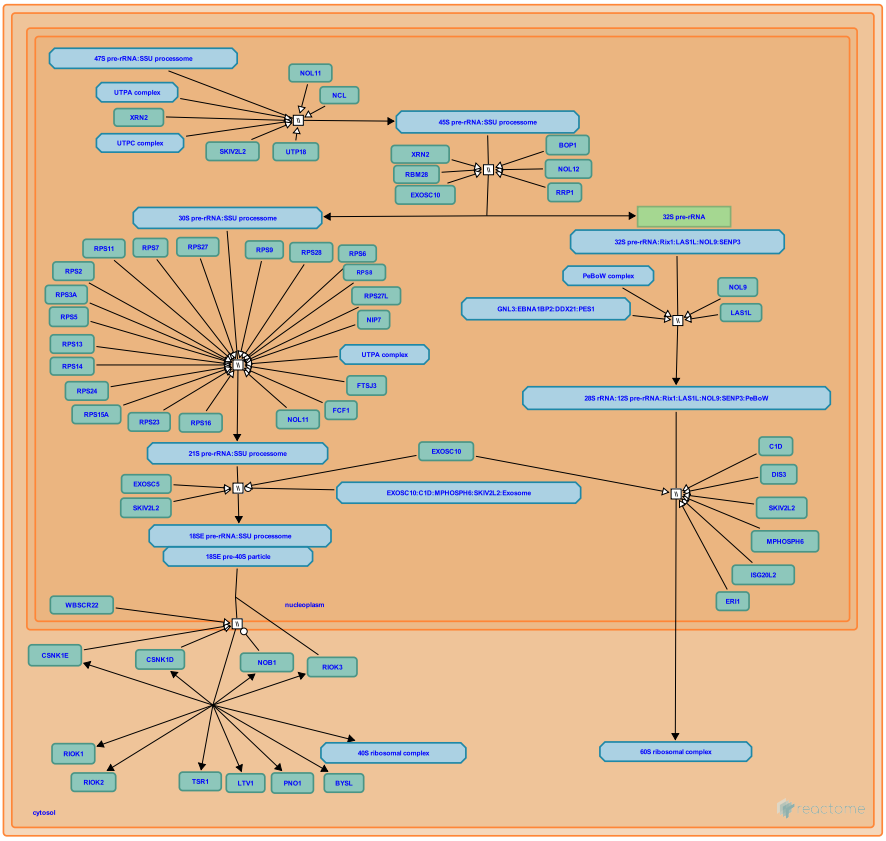
Major pathway of rRNA processing in the nucleolus and cytosol ↗

Location: rRNA processing in the nucleus and cytosol

Stable identifier: R-HSA-6791226



In humans, a 47S precursor rRNA (pre-rRNA) is transcribed by RNA polymerase I from rRNA-encoding genes (rDNA) at the boundary of the fibrillar center and the dense fibrillar components of the nucleolus (Stanek et al. 2001). The 47S precursor is processed over the course of about 5-8 minutes (Popov et al. 2013) by endoribonucleases and exoribonucleases to yield the 28S rRNA and 5.8S rRNA of the 60S subunit and the 18S rRNA of the 40S subunit (reviewed in Mullineus and Lafontaine 2012, Henras et al. 2015). As the pre-rRNA is being transcribed, a large protein complex, the small subunit (SSU) processome, assembles in the region of the 18S rRNA sequence, forming terminal knobs on the pre-rRNA (reviewed in Phipps et al. 2011, inferred from yeast in Dragon et al. 2002). The SSU processome contains both ribosomal proteins of the small subunit and processing factors which process the pre-rRNA and modify nucleotides. Through addition of subunits the SSU processome appears to be converted into the larger 90S pre-ribosome (inferred from yeast in Grandi et al. 2002). An analogous large subunit processome (LSU) assembles in the region of the 28S rRNA, however the LSU is less well characterized (inferred from yeast in McCann et al. 2015).

Following cleavage of the pre-rRNA within internal transcribed spacer 1 (ITS1), the pre-ribosomal particle separates into a pre-60S subunit and a pre-40S subunit in the nucleolus (reviewed in Hernandez-Verdun et al. 2010, Phipps et al. 2011). The pre-60S and pre-40S ribosomal particles are then exported from the nucleus to the cytoplasm where the processing factors dissociate and recycle back to the nucleus

Nuclease digestions of the 47S pre-rRNA can follow several paths. In the major pathway, the ends of the 47S pre-rRNA are trimmed to yield the 45S pre-rRNA. Digestion at site 2 (also called site 2b in mouse, see Henras et al. 2015 for nomenclature) cleaves the 45S pre-rRNA to yield the 30S pre-rRNA containing the

18S rRNA of the small subunit and the 32S pre-rRNA containing the 5.8S rRNA and the 28S rRNA of the large subunit. The 32S pre-rRNA is digested in the nucleus to yield the 5.8S rRNA and the 28S rRNA while the 30S pre-rRNA is digested in the nucleus to yield the 18SE pre-rRNA which is then processed in the nucleus and cytosol to yield the 18S rRNA. At least 286 human proteins, 74 of which have no yeast homolog, are required for efficient processing of pre-rRNA in the nucleus (Tafforeau et al. 2013)

Literature references

Henras, AK., Plisson-Chastang, C., O'Donohue, MF., Chakraborty, A., Gleizes, PE. (2015). An overview of pre-ribosomal RNA processing in eukaryotes. *Wiley Interdiscip Rev RNA, 6*, 225-42. ↗

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rRNA modification in the nucleus and cytosol ↗

Location: rRNA processing in the nucleus and cytosol

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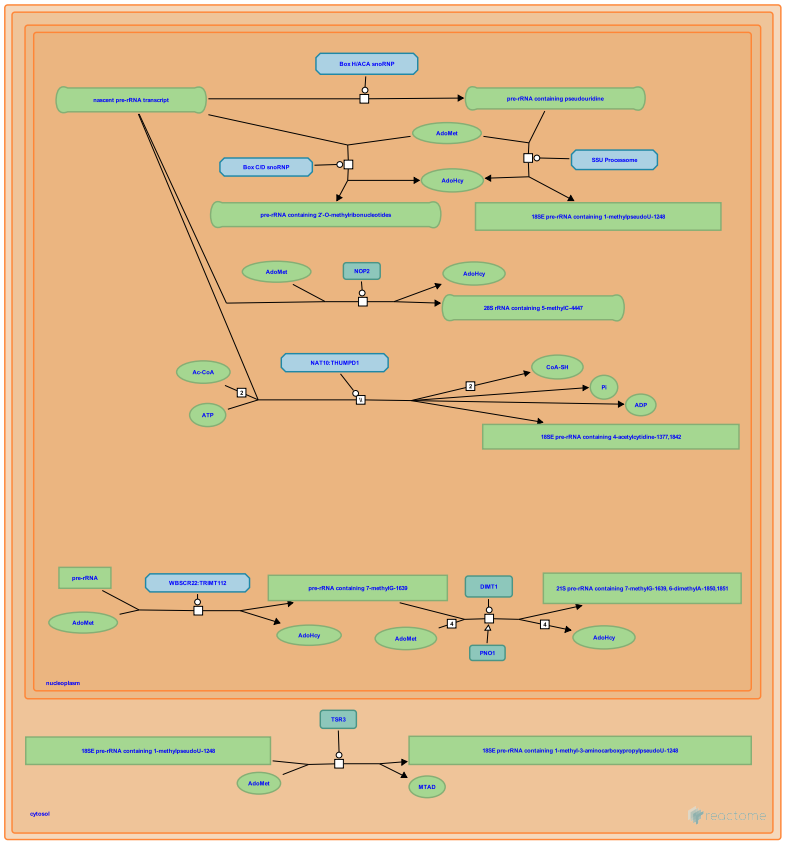

Human ribosomal RNAs (rRNAs) contain about 200 residues that are enzymatically modified after transcription in the nucleolus (Maden and Khan 1977, Maden 1988, Maden and Hughes 1997, reviewed in Hernandez-Verdun et al. 2010, Boschi-Muller and Motorin 2013). The modified residues occur in regions of the rRNAs that are located in functionally important parts of the ribosome, notably in the A and P peptidyl transfer sites, the polypeptide exit tunnel, and intersubunit contacts (Polikanov et al. 2015, reviewed in Decatur and Fournier 2002, Chow et al. 2007, Sharma and Lafontaine 2015). The two most common modifications are pseudouridines and 2'-O-methylribonucleotides. Formation of pseudouridine from encoded uridine is catalyzed by box H/ACA small nucleolar ribonucleoprotein (snoRNP) complexes (reviewed in Hamma and Ferre-D'Amare 2010, Watkins and Bohnsack 2011, Ge and Yu 2013, Kierzek et al. 2014, Yu and Meier 2014) and methylation of the hydroxyl group of the 2' carbon is catalyzed by box C/D snoRNPs (Kiss-Laszlo et al. 1996, Lapinaite et al. 2013, reviewed in Watkins and Bohnsack 2011). The snoRNP complexes contain common sets of protein subunits and unique snoRNAs that guide each complex to its target nucleotide of the rRNA by base-pairing between the snoRNA and the rRNA (reviewed in Henras et al. 2004, Watkins and Bohnsack 2011). Other modifications of rRNA include 5-methylcytidine (reviewed in Squires and Preiss 2010), 1-methylpseudouridine, 7-methylguanosine, 6-dimethyladenosine, and 4-acetylcytidine (reviewed in Sharma and Lafontaine 2015). In yeast most modifications are introduced co-transcriptionally (Kos and Tollervey 2010, reviewed in Turowski and Tollervey 2015), however the order of modification events and pre-rRNA cleavage events is not well characterized.

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