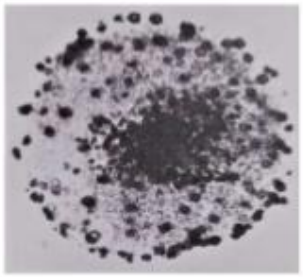
THE NUCLEOLUS

- The most prominent nuclear body is the nucleolus.
- It is the site of rRNA transcription and processing as well as aspects of ribosome assembly.
- The nucleolus is a ribosome production factory, designed to fulfill the need for regulated and efficient production of rRNAs and assembly of the ribosomal subunits.
- Actively growing mammalian cells, for example, contain 5 million to 10 million ribosomes that must be synthesized each time the cell divides.
- Recent evidence suggests that nucleoli also have a more general role in RNA modification and that several types of RNA move in and out of the nucleolus at specific stages during their processing.



Nucleoli in amphibian oocytes The amplified rRNA genes of *Xenopus* oocytes are clustered in multiple nucleoli (darkly stained spots).

RIBOSOMAL RNA GENES AND THE ORGANIZATION OF THE NUCLEOLUS

- The nucleolus is associated with the chromosomal regions that contain the genes for the 5.8S, 18S, and 28S rRNAs.
- Ribosomes of higher eukaryotes contain four types of RNA designated the 5S, 5.8S, 18S, and 28S rRNAs.
- The 5.8S, 18S, and 28S rRNAs are transcribed as a single unit within the nucleolus by RNA polymerase I, yielding a 45S ribosomal precursor RNA.
- Transcription of the 5S rRNA, which is also found in the 60S ribosomal subunit, takes place outside the nucleolus in higher eukaryotes and is catalyzed by RNA polymerase III.

IMPORTANCE OF RIBOSOME PRODUCTION

- The importance of ribosome production is particularly evident in oocytes in which the rRNA genes are amplified to support the synthesis of the large numbers of ribosomes required for early embryonic development.
- In *Xenopus* oocytes, the rRNA genes are amplified approximately two-thousand-fold, resulting in about one million copies per cell.
- These amplified rRNA genes are distributed to thousands of nucleoli, which support the accumulation of nearly 1012 ribosomes per oocyte.
- Recently, it has been shown that ribosome biogenesis is intimately linked to multiple cellular signaling pathways and that defects in ribosome production can lead to a wide variety of human diseases.

TRANSCRIPTION AND PROCESSING OF rRNA

- Each nucleolar organizing region contains a cluster of tandemly repeated rRNA genes separated from each other by non-transcribed spacer DNA.
- These genes are very actively transcribed by RNA polymerase I, allowing their transcription to be readily visualized by electron microscopy.
- In such electron micrographs, each of the tandemly arrayed rRNA genes is surrounded by densely packed growing RNA chains forming a structure that looks like a Christmas tree.
- The high density of growing RNA chains reflects that of RNA polymerase molecules, which are present at a maximal density of approximately one polymerase per hundred base pairs of template DNA.

RIBOSOME ASSEMBLY

- Early in ribosome assembly, the processing of the two nascent ribosomal subunits occur separately
- Processing of the smaller subunit, which contains only the 18S rRNA, is simpler and involves only four endonuclease cleavages.
- In higher eukaryotes, this is completed within the nucleus but in yeast the final cleavage to the mature 18S rRNA actually occurs after export of the 40S subunit to the cytosol.
- Processing of the larger subunit, which contains the 28S, 5.8and 5S rRNAs, involves extensive nuclease cleavages and is completed within the nucleolus. Consequently, most of the pre-ribosomal particles in the nucleolus represent precursors to the large (60S) subunit.
- The final stages of ribosomal subunit maturation follow the export of pre-ribosomal particles to the cytoplasm, forming the active 40S and 60S subunits of eukaryotic ribosomes.

Function of nucleolus

- Site for transcription
- Assemblage of ribosomes
- Synthesis of ribosomes
- Synthesis of RNA