Biogenesis of Ribosomes and Degenerative Disease: A review of the molecular mechanisms regulating ribosome function

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RIBOSOME BACKGROUND

Ribosome biogenesis occurs in all prokaryotic and eukaryotic organisms. Both differ in where biogenesis is occurs within the cell but the synthesis, processing, and assembly mechanisms remain the same (Alberts, 2022). Ribosomes (r) are characterized by their role in determining the translational ability of the cell, which is vital in regulating cellular processes including the maintenance of homeostasis, structural, and integrity e.g. metabolism and gene expression (Jiao, 2023). Their composition consists of ribonucleic acid (rRNA) and rProtein to produce two separate subunits, one small and one large (Alberts, 2022).

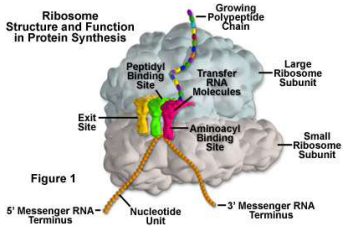

Figure 1. Three-dimensional structure of the large and small subunits making up a completed ribosome (Davidson, 2015).

DYSREGULATION PATHWAYS

Various factors that have direct impact on regulation and formation of biogenesis that increase the chances of mutation that eventually lead to cancer.

- **Intrinsic** how DNA transcription and RNA translation factors regulate ribosomal biogenesis through modifying processes necessary for transcription of rRNA.
- **Extrinsic** how extra and intracellular stressors such as nutrient availability and DNA damage can cause a stress response and can play a significant role in regulation of biogenesis.
- **Signaling** how certain cell talk and signal to one another using hormones, neurotransmitters, and various growth factors.
- **Epigenetic** how modifications to DNA, histones, and other regulatory elements impact the regulation of biogenesis through their association with rRNA transcriptional factors that can influence the expression of genes to either be on or off.

RIBOSOME DISCOVERY TIMELINE

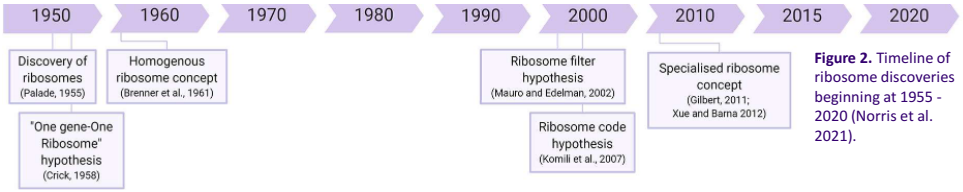

Figure 2. Timeline of ribosome discoveries beginning at 1955 - 2020 (Norris et al. 2021).

MOLECULAR MECHANISM OF BIOGENESIS

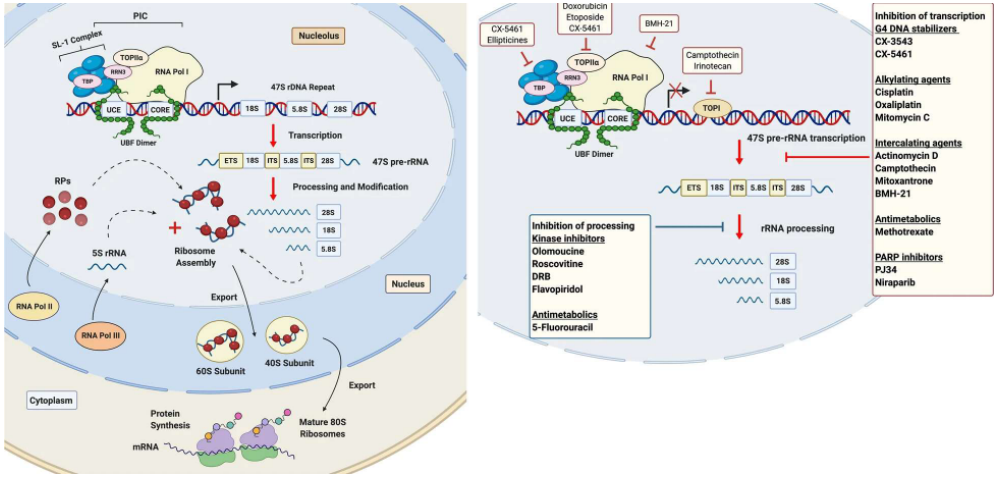

Figure 3. Ribosome biogenesis in mammalian cells (Steps 1-7)

1.Synthesis of DNA transcription to pre rRNA
2.Synthesis of rProtein
3.Processing of pre rRNA to mature rRNA
4.Processing of rProteins
5.Assembly mRNA and rProtein to form ribosomal subunits
6.Transport of the matured ribosomal subunits
7.Reassembly of the small and large ribosomal subunits to synthesize proteins
(Kang et al.2021) (Baweja et al.2021) (Turi et al. 2019)

CONCLUSIONS

•Ribosomal biogenesis involve synthesis, processing, and assembly of ribosomal subunits in the nucleus and cytoplasm.

•Completed ribosomes enable protein synthesis, cell growth, and stress response signaling feedback in a cell to occur.

•Dysregulation of ribosome biogenesis is linked to cancer formation.

•Our understanding of ribosomal biogenesis and its molecular mechanism is limited, and further research is needed in studying what influences the transcription and translation regarding during biogenesis.

•Utilizing our understanding of these processes can aid in developing treatments for degenerative diseases and improving quality of life for cancer patients.

FUTURE RESEARCH

•Genetic screening using CRISPR can be used to identify novel regulators of ribosome biogenesis and their impact on cancer development.

•Bioinformatics can be used to analyze a large datasets to identify gene expression patterns associated with normal and cancerous cells, aiding in the identification of risk factors that would be linked to cancer.

•Development of gene-targeted therapies can be used to provide potential treatments for those with dysregulated of ribosome biogenesis. Targeting and manipulating genes that are involved with dysregulation can restore normal function back in the ribosome to baseline function.

REFERENCES