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The role of intrinsically disordered regions (IDR) of RNA polymerase I machinery in nucleolar organization and chromatin compaction of ribosomal DNA

In eukaryotes, the nucleolus is a specialized nuclear compartment where the early stages of ribosome biogenesis take place. The nucleolar organization and ribosomal DNA compaction reflect ribosome production from yeast to human.

In yeast, ribosomal DNA is a unique 1-2 Mb region of chromosome XII in which 100-200 copies of ribosomal DNA (rDNA) are repeated. Ribosome assembly is initiated by massive transcription of rDNA by RNA polymerase I. In actively growing cells, rDNA is decondensed within the nucleolus, forming a crescent shape compartment occupying about one third of the entire nuclear volume. Upon growth inhibition, rDNA become rapidly condense, associated with global sub-nucleolar region re-organization. The underlying principle allowing such rapid and global re-organization of both rDNA and the nucleolus are poorly understood.

The nucleolus is enriched in protein bearing intrinsically disordered regions (IDRs). IDRs are protein domains exhibiting a high degree of conformational flexibility capable of forming low-energy interaction and thought to promote liquid liquid phase separation and condensate formation.

During my PhD, using yeast as model organism, we will investigate the putative role of IDRs of RNA polymerase I transcription machinery in nucleolar organization and compaction. Using live cells imaging and fluorescent labeled rDNA and nucleolar protein we will study the implication of IDRs deletion on nucleolar organization and rDNA compaction during either exponential growth or growth inhibition.

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