

Ribosome biogenesis "The Backstage".



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Ribosome biogenesis is an energetic expensive process which requires the synthesis of ribosomal RNA, ribosomal proteins and the action of more than 150 ribosome biogenesis factors. Most of the ribosome biogenesis factors are highly conserved proteins necessary for ribosome production which is essential for life. Indeed, mutations found in several human diseases map in genes coding for factors participating in early steps of ribosome biogenesis. Moreover, the action of some biogenesis factors has an impact on RNA polymerase I activity which is actually a target for cancer treatment. These early acting factors have been isolated as part of discrete protein complexes called UTP subcomplexes with a defined composition but unknown function. Thus, we consider the function of UTP subcomplexes as highly relevant, because it might involve putative regulatory mechanisms acting in the early events of ribosome biogenesis. In our initial studies, we have reconstituted yeast UTP subcomplexes using heterologous expression of their candidate components in insect cells. Our results suggest that formation of UTP subcomplexes is independent of ongoing ribosome biogenesis and likely triggered by the specific affinities between UTP components. Furthermore, we provide biochemical evidence about the existence of UTP building blocks as architectural elements of mature UTP subcomplexes. Our final goal is the mechanistic characterization of the early events in ribosome biogenesis. For this purpose, the use of *S. cerevisiae* as eukaryotic system and heterologous expression of factors from several organisms including humans will constitute the central axis of our research. Different *in vivo* and *in vitro* approaches will be discussed.