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Co-translational mechanisms regulate the synthesis of ribosomal proteins

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The biogenesis of a ribosome is a remarkably complex process involving more than 200 transient factors acting to assemble the 79 ribosomal proteins and four ribosomal RNAs that compose the yeast ribosome. A yeast cell must produce around 160'000 ribosomal proteins per minute to synthesise the 2'000 ribosomes required for sustaining a normal growth and division rate. This represents an incredible logistical achievement since most ribosomal proteins must travel from the cytoplasm, where they synthesised, to the nucleus, where they associate with the pre-ribosomal particles. Due to their interactions with negatively charged ribosomal RNA, most ribosomal proteins harbour positively charged basic residues making them prone to aggregation. Cells evolved general chaperoning systems to prevent such proteins from agglomerating and becoming troublesome for their wellbeing. In addition to these general mechanisms, some ribosomal proteins require protection by specific binding partners to be safely assembled into the pre-ribosomal particles. In the studies presented in this PhD thesis, we show that some of these dedicated chaperones, namely Acl4, Rrb1, Syo1, Sqt1, and Yar1, can capture their respective ribosomal protein partner co-translationally and accompany them to their assembly site. Not all of these dedicated chaperones are essential for the cell growth, but their absence causes dramatic defects in ribosome biogenesis. Interestingly, cells lacking *ACL4* accumulate spontaneous mutations that allow them to bypass the need of Acl4. We took advantage of these mutants to study the regulation of Rpl4 and unveil novel co-translational regulation mechanisms involving the nascent polypeptide-associated complex and the Ccr4-Not complex. Our findings give insight into the homeostatic regulatory mechanisms that monitor ribosome assembly and show how specific regulation of one ribosomal protein can be achieved with the help of both a dedicated chaperone and the general chaperoning system.

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