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Regulation of nuclear import of ribosomal proteins and ribosome assembly factors

Summary

Brigitte Pertschy, Institute of Molecular Biosciences

Supervisor:	PD Dr. Brigitte Pertschy
Availability:	This position is available.
Offered by:	University of Graz
Application deadline:	Applications are accepted between February 10, 2020 00:00 and March 30, 2020 23:59 (Europe/Zurich)

Description

Background: Ribosome biogenesis is a central metabolic process in all proliferating cells[1,2]. The first ribosome precursors are formed by the association of ribosomal proteins and ribosome assembly factors with ribosomal RNA (rRNA). The physical separation of the site of protein synthesis in the cytoplasm from the site of rRNA synthesis in the nucleolus necessitates mechanisms ensuring the efficient transport of ribosomal proteins and ribosome assembly factors from the cytoplasm into the nucleus. Nuclear import is mediated by import receptors (importins), which bind to nuclear localization sequences in their cargo proteins and mediate the transport into the nucleus. Moreover, importins can function as chaperones protecting their substrates from aggregation[3]. In our previous work, we found that in addition, ribosomal proteins are also guarded by dedicated ribosomal protein chaperones, a heterogenous group of proteins sharing the function of protecting ribosomal proteins from aggregation until they are incorporated into nascent ribosomes[4–7]. How nuclear import and chaperoning of ribosomal proteins is coordinated is so far poorly understood.

Hypothesis and Objectives: Based on our previous work, we hypothesize that post-translational modifications (including arginine methylation) modulate interactions between ribosomal proteins and their importin and chaperone binding partners. We suggest that by this means, post-translational modifications regulate nuclear import and chaperoning of ribosomal proteins and consequently influence the efficiency of ribosome biogenesis. We propose to use two ribosomal proteins and a ribosome assembly factor as models to study these mechanisms by:

Aim 1) generating mutants with increased and decreased levels of post-translational modifications and studying the resulting effect on nuclear import of ribosomal proteins and on the ribosome biogenesis pathway

Aim 2) studying the interactions between ribosomal proteins and importins and chaperones, as well as the influence of post-translational modifications on these interactions

Methodology: The PhD candidate will mainly use yeast as a model system to address these questions. The project will involve the genetic modification of yeast strains, cell biological experiments to evaluate the resulting phenotypes, and various biochemical assays to investigate protein-protein interactions.

References:

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4. Pillet, B., Mitterer, V., Kressler, D. & Pertschy, B. Hold on to your friends: Dedicated chaperones of ribosomal proteins: Dedicated chaperones mediate the safe transfer of ribosomal proteins to their site of pre-ribosome incorporation. *BioEssays News Rev. Mol. Cell. Dev. Biol.* **39**, 1–12 (2017).

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6. Mitterer, V. *et al.* Nuclear import of dimerized ribosomal protein Rps3 in complex with its chaperone Yar1. *Sci. Rep.* **6**, 36714 (2016).

7. Rössler, I. *et al.* Tsr4 and Nap1, two novel members of the ribosomal protein chaperOME. *Nucleic Acids Res.* (2019).

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