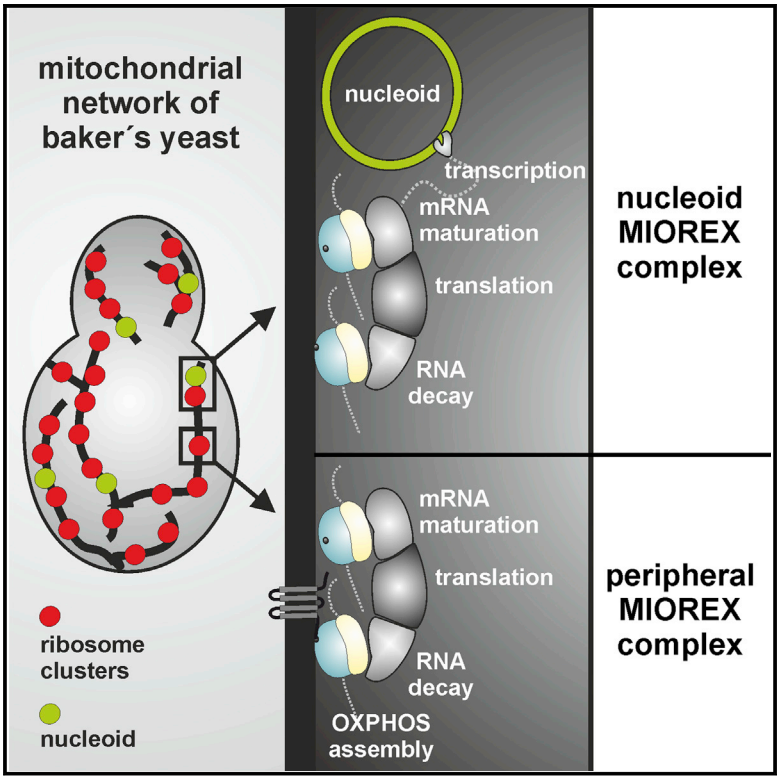
Cell Reports

Report

Organization of Mitochondrial Gene Expression in Two Distinct Ribosome-Containing Assemblies

Graphical Abstract



Highlights

- Mitochondrial ribosomes have a large interactome, resulting in MIOREX complexes
- MIOREX complexes organize ribosomes and mRNA metabolism in large assemblies
- A subset of the MIOREX complexes is associated with the nucleoid
- MIOREX complexes channel gene expression from transcription to translation

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In Brief

Mitochondria have a complete genetic system necessary for the biogenesis of the respiratory chain. Kehrein et al. utilize biochemical fractionation and superresolution microscopy to identify large clusters of mitochondrial ribosomes interacting with proteins implicated in posttranscriptional mRNA metabolism and respiratory chain assembly to create expressosome-like assemblies, the MIOREX complexes.

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Organization of Mitochondrial Gene Expression in Two Distinct Ribosome-Containing Assemblies

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SUMMARY

Mitochondria contain their own genetic system that provides subunits of the complexes driving oxidative phosphorylation. A quarter of the mitochondrial proteome participates in gene expression, but how all these factors are orchestrated and spatially organized is currently unknown. Here, we established a method to purify and analyze native and intact complexes of mitochondrial ribosomes. Quantitative mass spectrometry revealed extensive interactions of ribosomes with factors involved in all the steps of posttranscriptional gene expression. These interactions result in large expressosome-like assemblies that we termed mitochondrial organization of gene expression (MIOREX) complexes. Superresolution microscopy revealed that most MIOREX complexes are evenly distributed throughout the mitochondrial network, whereas a subset is present as nucleoid-MIOREX complexes that unite the whole spectrum of organellar gene expression. Our work therefore provides a conceptual framework for the spatial organization of mitochondrial protein synthesis that likely developed to facilitate gene expression in the organelle.

INTRODUCTION

Mitochondrial gene expression provides a small set of essential subunits to the oxidative phosphorylation system (OXPHOS) (Hällberg and Larsson, 2014). Proteins involved in expression and assembly of the mitochondrially encoded translation products represent a quarter of the mitochondrial proteome of baker's yeast (Sickmann et al., 2003), and this genetic system contains complete machineries for DNA replication, repair, and transcription; for RNA modification, mRNA maturation/splicing, and RNA degradation; and for protein synthesis. How these proteins cooperate to mediate efficient protein synthesis and how they are organized in time and space is currently not known.

Mitochondrial ribosomes developed from those of the bacterial ancestor of the organelle and were significantly remodeled during evolution; they contain many mitochondria-specific protein subunits and have a reduced rRNA content (Kehrein et al., 2013; Smits et al., 2007). This modified composition was accompanied by the development of mitochondria-specific features of translation. Prime examples for this are specific translational activators that are required for translation of a single species of mRNA (Costanzo and Fox, 1990; Fox, 2012). Recent work has demonstrated that translational activators coordinate mitochondrial and nuclear gene expression to facilitate biogenesis of the OXPHOS (Gruschke et al., 2012; Mick et al., 2011). In the case of cytochrome *b* biogenesis, this feedback loop involves binding of a translational activator complex to the ribosomal tunnel exit to enable efficient interaction of the newly synthesized protein with an assembly factor (Gruschke et al., 2011).

Because of this rather unique organization of protein synthesis in mitochondria, we asked how mitochondrial ribosomes are generally organized and whether factors involved in the biogenesis of the other mitochondrially encoded proteins also interact with the mitochondrial ribosome. We established a method to purify and analyze native and intact mitochondrial ribosome complexes. Mass spectrometric analyses revealed extensive interactions of this translation machinery with factors involved in various posttranscriptional steps of gene expression. Likewise, we identified many proteins without annotated function. Employing biochemical fractionations and superresolution microscopy, we show that mitochondrial ribosomes are forming distinct clusters that we term mitochondrial organization of gene expression (MIOREX) complexes. A subset of these clusters is engaged in a large complex with the nucleoid that unites transcription, mRNA maturation, translation, and RNA decay. The organization