Publications

1. Mustafa Malik-Ghulam**,** Mathieu Catala, Michelle Scott and Sherif Abou Elela. Specialized ribosomal protein genes promotedrug resistance through selective modulation of translation. Under revision in **Molecular Cell.**
2. Mustafa Malik-Ghulam, Mathieu Catala and Sherif Abou Elela. Differential expression of duplicated ribosomal protein genes modifies ribosome composition in response to stress. Under revision in **Nucleic Acid Research (NAR).**
3. Malik Ghulam et al., Peptide based quantification of duplicated ribosomal proteins (dRPs) in *S. cerevisiae* using Swath MRM coupled with dialysis and lyophilisation. **In preparation.**
4. Parenteau J., Lavoie M., Catala M., Malik-Ghulam M., Gagnon J., Abou Elela S., Preservation of Gene Duplication Increases the Regulatory, Spectrum of Ribosomal Protein Genes and Enhances Growth under Stress. **Cell Reports**. 2015 Dec 22;13(11):2516-2526.

Book chapters

1. Malik Ghulam M, M.Khan Md G., Nguyen D., Iqbal S., "Techniques in Biotechnology: Essential for Industry". Omics Technologies and Bio-Engineering Volume 2: Towards Improving Quality of Life 2018, Pages 233-249. **Elsevier Inc.**
2. Malik Ghulam M.**,** Kousar S., and Vardhan H., Mitochondrial Omics: State-of-the-Art Knowledge. PlantOmics: The Omics of Plant Science. 2015 pages (573-613). **Springer Books.**

Bourses, Prix & Distinctions

Sept 2018	1st Prize for poster presentation - Riboclub, Orford Quebec Canada.
May 2014	3rd prize for poster presentation – Scientific day of the Faculty of Medicine and Health Sciences, Université de Sherbrooke, Quebec Canada.
2013	Bourses aux études supérieures, Innople, Faculté de Médécine, Université de Sherbrooke.

UNIVERSITÉ DE SHERBROOKE

Études supérieures
Faculté de médecine et des sciences de la santé

SOUTENANCE DE THÈSE

DOCTORAT EN MICROBIOLOGIE

MUSTAFA MALIK GHULAM

Vendredi, le 22 novembre 2019
14H00
Z8-1050 (Amphithéâtre-PRAC)

Functional Analysis of Duplicated Ribosomal Protein Genes in *Saccharomyces cerevisiae*

Résumé

The ribosome is an essential ribonucleoprotein complex required for protein synthesis. In *Saccharomyces cerevisiae*, 75 % of the ribosomal protein genes are duplicated (dRPGs) and 62 % of these dRPGs produce proteins that differ by one or more amino acids (non identical dRPs). It was initially proposed that duplication of RPGs may be meant for dosage purposes only. Later a “ribosome code” was proposed which states that these dRPGs are the bases of a ribosome code permitting the cell to modulate its ribosomal contents in response to changes in growth conditions. However, the mechanism regulating the expression of these dRPGs and the function of this proposed code remains largely unknown.

We monitored different levels of dRPG expression by RNAPII ChIP-Seq, RNA-seq, mRNA association to polyribosomes, and peptide-based mass-spectrometry to determine paralog specific transcription potential, splicing, mRNA abundance, translation, protein abundance and incorporation in the actively translating ribosomes before and after exposure to stress. Under normal conditions, expression hierarchy of the dRPGs is co-transcriptionally established through efficient splicing, high stability and efficient translation of the major paralog mRNA. Exposure of the cell to stress modifies the expression ratio of the paralogs by repressing the expression of the major paralog and thus increasing the number of ribosomes carrying the minor paralog leading to modification of translation pattern and increased resistance to drug. Expression of the more expressed (major) paralog of uL30/RPL7 increased cell sensitivity to staurosporine while expression of the less expressed (minor) paralog induced resistance. Remarkably, we found that difference in paralogs function was due to difference in the translation pattern. The minor paralog promoted the translation of cell wall genes with long open reading frames (ORFs), which are normally under-translated in the presence of the major paralog, leading to drug resistance. Reducing the ORF length repressed the effect of minor paralog and staurosporine on translation. Together the data reveal a natural mechanism for the optimization of translation through changes in the identity of ribosomal protein genes.

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