

Transcriptional Regulation Network of Ribosomal Protein Genes in Yeasts

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Expression of RPGs is a major energy consuming process; more than 50% of total transcription is devoted to RP genes. It has been well known that highly ordered expressions of ribosomal protein genes are mostly regulated in the transcription level in yeast. However, these genes are scattered throughout the genome in all eukaryotes and their promoter architectures are different from each other. Therefore, there must exist a mechanism for a gene regulation network. But little is known about this in yeasts. Recently, it has been found that many ribosomal proteins have multiple functions besides protein synthesis. These extra-ribosomal functions include post-transcriptional gene regulation, DNA replication, repair and apoptosis. We are currently investigating the ribosomal gene regulation using extra-ribosomal functions of ribosomal proteins. In many researches, there are many signaling pathways such as ‘Target Of Rapamycin’ (TOR), ras-cAMP-protein kinase A (PKA) and secretory pathway participated on the regulation of these genes. Here, we examined the specific transcriptional regulation of RPGs in *Saccharomyces cerevisiae* and *Candida albicans* during environmental stress.

In *S. cerevisiae*, most RP promoters were reported to contain the binding site of Rap1p (UASrpg), which is important for the adequate transcription to meet cellular needs. However, it does not appear to play a role as a specific regulator because it is a context dependent transcriptional regulator. To find putative specific transcriptional regulators of RP gene transcription, we examined binding partners of Rap1p by TAP purification and found that Gcn4p directly binds to Rap1p at the RP promoters. Our studies identify a novel role of Gcn4p on the transcription of RPGs under amino acid starvation.

The human fungal pathogen *Candida albicans* switches its morphology from a yeast form to a hyphal form when it infects a host. We analyzed the RPGs expressions during the morphological transition state. Transcriptions of all RPGs checked in here were decreased under hyphal growth condition, and similar down regulation was detected only in a constitutive hyphal growing strain. It was also found that the levels of polysome and monosome were decreased during the filamentous growth. Interestingly, it was revealed that all these phenomena were mediated by TOR1 kinase. From these results, we suggested that there is a cross-talk between TOR1-dependent ribosome biogenesis and morphological transition signaling pathways in *Candida albicans*. Moreover, we found that one of ribosomal protein, Asc1p plays a pivotal role in regulating the expression of several genes some of which are important for virulence of *C. albicans*.

Taken together, we suggested that yeast delicately regulates the RPGs transcription and ribosome biogenesis to save available resources and energy under various environmental stress conditions, and this could make yeasts adapt or overcome harsh conditions for their surviving.