NISR RESEARCH GRANT
2002 Young Investigator Research Grant

Selective Nuclear Export of mRNAs under Stressed Conditions in *Saccharomyces cerevisiae*

Shingo IZAWA

Division of Applied Life Science, Graduate School of Agriculture, Kyoto University

It is well known that cells show adaptive stress responses both at the transcriptional level and the translational level under stressed conditions. Recently, it has been reported that adaptive responses are also induced at the level of mRNA export from the nucleus to the cytoplasm. Several stresses such as heat shock and ethanol stress cause selective mRNA export in *Saccharomyces cerevisiae*. Bulk poly $(A)^+$ mRNAs accumulate in the nucleus, whereas mRNAs of heat shock proteins are exported under stressed conditions. However, the mechanisms of mRNA export still remain to be clarified, and we have little information about the selective export of mRNAs under stressed conditions. In this study, we investigated the response to stresses including high salt stress in mRNA export in yeast cells. We also investigated the changes in mRNA export factors under stressed conditions. Through this research, we got several novel and interesting findings about stress responses in mRNA export.

Export of mRNAs under high salt stressed conditions in yeast

We investigated the export of bulk poly $(A)^+$ mRNAs under stressed conditions by *in situ* hybridization using oligo dT probes. In *S. cerevisiae*, high salt stress (0.4 M NaCl) rapidly blocked the export of bulk poly $(A)^+$ mRNAs and induced the accumulation of poly $(A)^+$ mRNAs in the nucleus. On the other hand, the *ENA1* mRNA, a high salt stress responsive gene, was synthesized and exported to the cytoplasm under high salt stressed conditions. Intriguingly, the export of bulk poly $(A)^+$ mRNAs was resumed approximately 5 min after the treatment with high salt stress, whereas heat shock and ethanol stress blocked the export of bulk poly $(A)^+$ mRNAs over 1 hour. Furthermore, the nuclear accumulation of mRNAs under 1.0 M NaCl was not induced by the pretreatment with mild salt stress (0.1 M NaCl for 1 hour). These results indicate that the adaptation to high salt stress in mRNA export is presumably induced easily and rapidly in *S. cerevisiae*. We also investigated the mRNA export in *Zygosaccharomyces rouxii*. Bulk poly $(A)^+$ mRNAs were exported even under 1.0 M NaCl and no accumulation of mRNAs in the nucleus was induced in *Z. rouxii*, indicating that *Z. rouxii* has higher ability to adapt to high salt stress also in mRNA export. We are now trying to identify other mRNAs exported under high salt stressed conditions as well as *ENA1* in *S. cerevisiae*. The cloning of genes encoding mRNA export factors of *Z. rouxii* is also underway.

Stress responsive changes in the localization of mRNA export factors

We investigated the effects of stresses on mRNA export factors. Several export factors and nucleoporins showed the changes in their localizations under stressed conditions. One of the export factors, Rat8p, showed the stress response to ethanol but not to other stresses. In yeast cells treated with ethanol stress, Rat8p showed reversible and rapid change in its localization, indicating that the blocking of bulk poly $(A)^+$ mRNAs export under ethanol stressed conditions is partly caused by the stress-responsive change in the localization of Rat8p. Intriguingly, Rat8p did not change its localization under heat shocked conditions, suggesting a possibility that mechanisms of the blocking of mRNA export are different between ethanol stressed conditions and other stressed conditions. We also found that Rat8p is dispensable for the export of stress inducible mRNAs under ethanol stressed conditions. This is the first report of the stress-responsive changes in the localization of mRNA export factors. These results may aid understanding of the contribution of mRNA export factors to selective mRNA export under stressed conditions.

Reference

Shingo Izawa, Reiko Takemura, and Yoshiharu Inoue. Stress Response in Yeast mRNA Export Factors: Reversible Change in the Localization of Rat8p Is Caused by Ethanol Stress but Not by Heat Shock. (submitted)