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Abstract

Cells continuously create and degrade proteins. Some proteins are made in the cytoplasm and need to be transported into the endoplasmic reticulum. To complete this task, proteins move through a channel called the translocon in a process called translocation. Mutations in the translocon are associated with multiple human diseases, including diabetes and immune disorders. Translocation may occur co-translationally or post-translationally. Occasionally, the mRNA encoding a protein will aberrantly lack a stop codon, which results in translation of the 3' untranslated region and ribosomal stalling if a stop codon is not fortuitously encountered. If the protein is ER-targeted, the protein will also stall within and clog the translocon. The ubiquitin ligase Rkr1 (which is conserved from yeast to humans) recognizes when a ribosome is stalled, and ubiquitylates the polypeptide chain stalling in the ribosome and translocon, resulting in its proteasomal degradation. By contrast, the protease Ste24 (also conserved from yeast to humans) cleaves proteins that are stalled in the translocon post-translationally. The aim of this study is to test the hypothesis that Ste24 acts upon co-translationally stalled polypeptides, using budding yeast as a model organism. The hypothesis is being tested via western blot analysis in which abundance of model translationally stalled translocon-clogging protein is compared in wild type cells, cells lacking Rkr1, and cells lacking Ste24. Initial findings suggest that Ste24 does not act upon co-translationally stalled proteins at the translocon. These results indicate a high substrate specificity for the enzymes that target translocon-clogging proteins.

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