Krótkie niekodujące RNA (tRF i sdRNA) asocjujące z rybosomami w *Saccharomyces cerevisiae* – geneza i funkcje regulatorowe w zróżnicowanych warunkach środowiskowych

Anna Maria Mleczko

Abstract

Development of deep sequencing and high-throughput techniques has led to the discovery of a wide range of non-coding RNA molecules (ncRNAs). These molecules play key roles during regulation of gene expression and they shape cellular life. In recent years it has been shown that under certain conditions non-coding RNAs may become precursors of shorter RNAs. This relatively new topic is currently the object of intense research. The existence of many unknown mechanisms that regulate important functions of cells, such as stress response, metabolism or cell cycle has recently been shown. Lately, the existence of a new protein biosynthesis regulation pathway was discovered. It has been shown that translation may be regulated by direct association of short RNAs with ribosomes in baker′s yeast *Saccharomyces cerevisiae*. Short RNAs which associate with the ribosome are named ribosome-associated noncoding RNAs (rancRNAs). Among rancRNAs, many new classes of short RNAs have been detected. These RNAs arise during stress conditions by processing of a well-known non-coding RNAs such as snoRNA, rRNA, mRNA or tRNA.

The aim of this study was to extend the knowledge about rancRNAs, with particular emphasis on two classes of rancRNAs: tRFs (tRNA-derived fragments) and sdRNAs (snoRNA-derived RNAs). I have examined stress-dependent processing of tRNAs and snoRNAs to shorter RNAs, performed analysis of their association with ribosomes and studied the potential function of tRFs and sdRNAs in yeast *S. cerevisiae*.

At initial steps of work, I have focused on short RNAs derived from tRNAs. I have examined stress-dependent cleavage of tRNAs to tRFs. The results showed that global tRF pool remains unchanged, regardless of the environmental conditions in which yeast *S. cerevisiae* was grown. The next step was to examine the functions of selected tRFs. I have shown that six ranc-tRFs are capable of decreasing the level of global protein biosynthesis at the tRNA aminoacylation level. tRFs achieve this by direct association with the ribosome and aminoacyl-tRNA synthetases.

Subsequently, the cleavage and subcellular localization of snoRNAs and sdRNAs were examined. I have found that both sdRNAs and their precursors, snoRNAs, are present in the cytoplasm and their abundance depends on stress conditions. Moreover, I showed that both snoRNAs and sdRNAs associate with translationally active ribosomes and thus sdRNAs may regulate protein biosynthesis *in vitro*.

The results presented in this doctoral dissertation have been published in four peer-reviewed experimental articles. Issues regarding processing of snoRNAs to sdRNAs and their functions are described and summarized in the review, which is also part of this doctoral dissertation.