Streszczenie w języku angielskim

The production of recombinant proteins (r-Prots) is one of the key areas of modern biotechnology. Among a number of microbial producers of r-Prots, the *Yarrowia lipolytica* yeast species is gaining high interest due to many relevant and beneficial features. For years, work has been carried out in the field of genetic engineering on the improvement of *Y. lipolytica* strains in order to intensify the synthesis and secretion of r-Prot. Acquiring new, detailed knowledge on the functioning of the translational-secretory pathway will allow for the refinement of the modification strategies being developed. The translational-secretory pathway is a multifunctional, integrated, multi-organelle network of structural and functional interaction. Hence, under high levels of r-Prots overproduction, dysfunction at one point affects the functioning of a wide spectrum of molecular events in the cell. Overproduction of secretory-Prots (rs-Prots) frequently leads to an overload of cellular mechanisms and induces severe stress, which in turn leads to the loss of the target protein. Global knowledge of the elements, as well as an understanding of the biological processes involved in the folding, maturation and secretion of polypeptides and their interrelationships, is possible thanks to the development of omics analysis. Considering that the global r(s)-Prots market is one of the key branches of the modern biotechnology industry, research on the biology of the translational-secretory pathway is important from the point of view of basic and applied sciences.

This work aimed at describing the elements and mechanisms of the translational-secretory pathway operation in *Y. lipolytica*. To endow the experimental set-up with an inert character, the tested strains overproducing r(s)-Prots were maintained in a steady state. Strains overproducing r(s)-Prots with different biochemical properties were analyzed to identify elements and mechanisms specific to a given biological process (such as glycosylation, oxidative folding, etc.). The experimental set-up prepared in this way was then subjected to global transcriptomic analysis. Detailed analysis of the omics data provided insight into the biological processes taking place in the cell, including initiation of oxidative stress and unfolded protein response (UPR), as well as identification of elements involved in the process of glycosylation, folding and translocation of r(s)-Prots. Particularly interesting observations were made on the functioning of the unconventional protein secretion mechanism, the involvement of transcription regulators, the initiation or inhibition of vacuolar proteolysis, or the arrest of cell cycle progression. Based on the omics data, some of the identified genes were used as helper factors for the synthesis and secretion of rs-Prots.

The results of this experiment clearly showed that co-overexpression of the helper genes significantly increased the efficiency of target protein synthesis by *Y. lipolytica*, which was dependent on the adopted culture temperature. In addition, a detailed analysis of the molecular mechanisms induced under co-overexpression of the key transcription factor involved in the initiation of the UPR response - Hac1, was performed. It was shown that the co-expression of native *HAC1* improves the secretion of rs-Prots and significantly affects the deregulation of genes involved in ribosome biogenesis, processes occurring in the cell nucleus and mitochondria, cell cycle arrest, as well as modulation of proteolysis and RNA metabolism.

The results obtained in this work contributed to a better understanding of the biology of r(s)-Prots synthesis and secretion in *Y. lipolytica* cells. The acquired knowledge enabled the development of an effective strategy of genetic modification of these yeasts in order to intensify the production of rs-Prots in the cells of this host.

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