Streszczenie w języku angielskim
rozprawy doktorskiej mgr inż. Moniki Kubiak-Szymendery pt. „Manipulacje komórkową odpowiedzią na stres jako strategia zwiększająca nadprodukcję heterologicznych białek w rekombinowanych komórkach drożdży niekonwencjonalnych *Yarrowia lipolytica*"

Strategies for intensification of the biotechnological production of recombinant proteins (r-Prots) can relate to both the genetic manipulation of the host organism and the optimization of the bioprocess conditions. The execution of stress conditions at appropriate intensity and period may have a beneficial effect on the production of various compounds, including recombinant secretory proteins (rs-Prots).

In this study, this hypothesis was tested with regard to selected environmental stress factors and rs-Prot synthesis in cells of the nonconventional yeast *Y. lipolytica*.

The conducted research provides evidence for positive impact of temporary exposure to lowered temperature on the production of rs-Prot by *Y. lipolytica*. Both time and temperature were found significant for the obtained effects. Optimized thermal treatment conditions were applied to the process carried out with technical substrates and crude glycerol. No loss in the enzyme production was observed due to exploitation of the alternative substrates, and the development of the pilot-scale waste-free process model allowed to assess actual economic gain from the exchange of substrates, and to identify bottlenecks of the process.

Within the framework of the conducted research, the effect of osmotic pressure executed by the addition of different osmoactive compounds on the production of rs-Prot was investigated. Preliminary studies indicated their promoting effect on the production of rs-Prot, however, no correlation was observed between osmolality and the specific activity of rs-Prot, and the chemical character of the used osmoactive compound played a key role. Further in-depth research contradicted these preliminary observations.

In order to gain knowledge about the molecular basis of the observed phenomena, the physiological, transcriptional and proteomic responses of the recombinant *Y. lipolytica* strain overproducing rs-Prot were analysed, when exposed to selected stress factors: ↑Osm, ↓Temp and ↑Osm↓Temp. The executed hyperosmolality did not increase the synthesis of rs-Prot, but only its transcription. The overrepresented proteins included heat shock proteins (HSPs) and aldo-keto reductases (AKRs), but the processes related to protein synthesis and central carbon metabolism were limited by ↑Osm. Significantly, the ↓Temp treatment did not cause any significant changes at the proteome level, and in combination with hyperosmolality (↑Osm↓Temp), the lowered temperature contributed to reduction of the negative effects of ↑Osm.

Epigenetic studies on *Y. lipolytica* cells treated with high temperature (↑Temp) and sequentially subcultured (RB) provided further information on the physiological response of this yeast species to environmental stresses. No epigenetic response of *Y. lipolytica* to the executed heat stress was observed, but a general phenomenon of a decrease in the level of genome methylation in the stationary phase compared to the epigenome of the late exponential phase of growth was identified, as well as a significant impact of the repeated subculturing on the global level of genome methylation.

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