From transcriptomic profiling to engineering target selection in *Haloferax mediterranei* for PHBV and bacterioruberin production

Ivelina Ivaylova Dzhambazova[1], Simona Varriale[1], Pierluigi Gabriele Di Matteo[1], Luigi Aurino[1], Alessandra Coletta[1], Cinzia Pezzella[1]

[1] *Department of Chemical Sciences, University of Naples "Federico II", Naples, Italy*

Ivelinaivaylova.dzhambazova@unina.it

Haloferax mediterranei is a promising archaeal platform for next-generation industrial biotechnology, owing to its natural ability to synthesize both poly(3-hydroxybutyrate-*co*-3-hydroxyvalerate) (PHBV), a promising PHA-copolymer, and bacterioruberin, a rare C-50 carotenoid [1]. Since the accumulation of these compounds is promoted by distinct cultivation conditions, understanding how carbon flux is redistributed between the two pathways is essential for rational strain engineering. In this work, transcriptomic profiling was performed on *H. mediterranei* cultivated under different conditions identified by statistical optimization as favoring either PHBV or bacterioruberin production [2]. Differential expression analysis highlighted condition-specific regulatory and metabolic responses linked to carbon flux distribution, precursor supply, and carotenoid biosynthesis.

The integration of transcriptomic data with pathway knowledge enabled the selection of candidate targets for metabolic engineering. For PHBV-oriented strategies, *korAB* and *porAB* were identified as relevant targets associated with propionyl-coA supply, while *cimA* was selected for promoter engineering to further modulate precursor flux. For bacterioruberin-oriented strategies, *lyeJ* emerged as a candidate target from transcriptomic analysis, and promoter engineering of *crtB* and *crtI* was designed to modulate flux through the carotenoid biosynthetic pathway. These results establish a transcriptomics-guided framework for target prioritization in *H. mediterranei* and support ongoing engineering efforts aimed at improving PHBV and bacterioruberin production.

References

[1] D. B. Griffiths *et al.* 2025, doi: 10.1016/j.biotechadv.2025.108666

[2] E. Borselleca *et al.* 2025, doi: 10.1016/j.scp.2025.102137

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