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Evaluation of metabolic redox homeostasis in prokaryotes

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The work focuses on cellular redox homeostasis in prokaryotic micro-organisms, and specifically on factors associated with nicotinamide adenine cofactor [NADP(H) and NAD(H)] metabolism in *E. coli* and photoautotrophic cyanobacterium *Synechocystis sp.* PCC 6803. These cofactors participate in numerous electron transfer reactions in the cell, linking enzymatic reactions with the overall energy metabolism with biosynthetic reactions and housekeeping functions. Obtaining a comprehensive view of the interactions and the regulatory circuits is thus of central importance in understanding the adaptation to different environmental conditions, such as those involved with the transition between autotrophic and heterotrophic growth modes in cyanobacteria.

The principal objective is to study the role of the proton gradient-coupled pyridine nucleotide transhydrogenase PntAB. Functional characterization combined with structural modelling of PntAB in *Synechocystis sp.* PCC 6803 has been carried out¹, and information-rich networks have been created to identify novel candidates involved in the NADP(H)-regulation in different organisms². In addition, PntAB is studied through deletion and over-expression mutants under anaerobic fermentative conditions and under different pH's in *E. coli*. Specifically, the initiative is to elucidate to what extent the regulation of the cofactor redox balance takes place at the level of alternative catabolic routes in glucose breakdown, and what is the role of *PntAB* under these specific conditions. The approach is to generate pntAB over-expression and knock-out strains, and to compare them in phenotypic growth properties as well as in respect to changes in the central carbon metabolism by analyzing the distribution of local ratios of amino acids using C¹³ labelled glucose as a probe.

1. Kämäräinen, J.; Huokko, T.; Kreula, S.; Jones, P. R.; Aro, E. M.; Kallio, P., Pyridine nucleotide transhydrogenase PntAB is essential for optimal growth and photosynthetic integrity under low-light mixotrophic conditions in *Synechocystis sp.* PCC 6803. *New Phytol* 2017, 214 (1), 194-204.
2. Kreula, S. M.; Kaewphan, S.; Ginter, F.; Jones, P. R., Finding novel relationships with integrated gene-gene association network analysis of *Synechocystis sp.* PCC 6803 using species-independent text-mining. *PeerJ* 2018, 6, e4806.

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