An enhanced electron transport chain improved astaxanthin production in Phaffia rhodozyma

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Abstract

Astaxanthin (AX) is a carotenoid pigment with antioxidant properties. AX is used widely in the animal feed industry as a supplement. Wild-type strains of Phaffia rhodozyma naturally produce low AX yields, but we increased AX yields 50-fold in previous research using random mutagenesis of P. rhodozyma CBS6938 and fermentation optimisation. Genome sequencing linked phenotype and genome changes of the increased AX production but relevant metabolic changes were not resolved. In this study, the wild-type and the superior P. rhodozyma mutant strains were grown in chemically defined media and instrumented fermenters. Differential kinetic, metabolomics, and transcriptomics data were collected. Our results suggest that carotenoid production was mainly associated with cell growth and had a positive regulation of central carbon metabolism metabolites associated with glycolysis, the pentose phosphate pathway, the TCA cycle, and amino acids and fatty acids biosynthesis. In the stationary phase, amino acids associated with the TCA cycle increased, but most of the fatty acids and central carbon metabolism metabolites decreased. TCA cycle metabolites such as succinate, fumarate, and α-ketoglutarate were in abundance during both growth and stationary phases. The overall observed metabolic changes in the central carbon metabolism and abundance of TCA cycle metabolites suggest an improvement in the electron transport chain and the provision of the electrons required for the AX synthesis. Transcriptomic data correlated with the metabolic data and found a positive regulation of genes associated with the electron respiratory chain suggesting this to be the main driver for improved AX production in the mutant strain.

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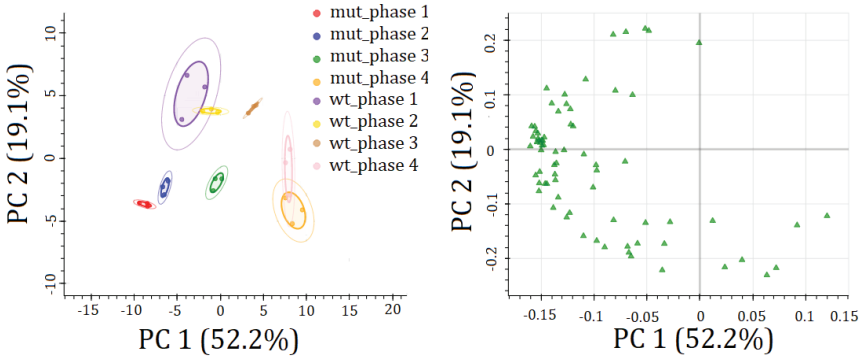

Mutant/Wild-Type

Amino Acids

Metabolite	Phase 1	Phase 2	Phase 3	Phase 4
Arginine				
Histidine				
Threonine				
Glutamine				
Lysine				
Valine				
Methionine				
Isoleucine				
Leucine				
Phenylalanine				
Tryptophan				
L-Tyrosine				
Proline				
Serine				
Aspartic acid				
Glutamic acid				
Glycine				
Asparagine				
Alanine				

Central Carbon Metabolism

PYR				
FUM				
SUC				
KGA				
PEP				
DHAP				
3PG_2PG				
CIT				
RL5P				
R5P				
G1P				
G6P				
F6P				
F16DP				
Glyox				
Mal				
GA3P				
GMP				
UDP				
ADP				
GDP				
ATP				
GTP				
CMP				
UMP				
AMP				
NADPH				
cAMP				
UDPGA				
NAD				
NADH				
NADP				
UDPNAc				
ACO				

Fatty Acid Methyl Esthers

C4:0				
C8:0				
C10:0				
C12:0				
C14:0				
C14:1				
C15:0				
C15:1				
C16:0				
C16:1				
C17:0				
C17:1				
C18:0				

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