
Major role of the post-transcriptional CSR system in the regulation of *E. coli* metabolism

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Abstract

Understanding of *Escherichia coli* metabolic properties is essential to master bacterial proliferation and capacities and is a prerequisite for its efficient use in synthetic biology applications. Metabolic control in *E. coli* is a complex process involving multi-level regulatory systems but the involvement of post-transcriptional regulation is uncertain.

The post-transcriptional factor CsrA is stated to be involved in the regulation of many important cellular functions (central carbon metabolism, virulence, biofilm, stringent response...). However only a few targets has been identified and their impact on the metabolism functioning has not been demonstrated.

To investigate the post-transcriptional role of CsrA in regulating metabolism, a multi-scale analysis (including genome-wide measurements of mRNA stability and level but also growth parameters, metabolite pools, abundance of enzymes and modelled fluxes) was performed in wildtype *E. coli* (MG1655) and in an isogenic mutant strain deficient in CsrA activity (1,2). We demonstrated for the first time that CsrA is a global positive regulator of mRNA stability. For one hundred genes, we predicted that direct control of mRNA stability by CsrA might contribute to metabolic adaptation by regulating expression of genes involved in carbon metabolism and transport. Focusing on the central carbon metabolism, the CSR system was essential for the effective functioning of the upper glycolysis mainly through its control of the phosphofructokinase enzyme (PfkA). Indeed, an imbalance of metabolite pools in the upper glycolysis, before the PfkA step was observed in the *csrA* mutant. This imbalance was associated with a glucose-phosphate stress and was suppressed by restoring PfkA activity in the *csrA* mutant strain.

This work demonstrates the pivotal role at the post-transcriptional level of the CSR system to shape the carbon metabolism and more largely the whole metabolism which is essential for driving the bacterial adaptation.

References

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