# Characterization of a transcription factor involved in the regulation of β-alanine metabolism in the hyperthermoacidophilic archaeon *Sulfolobus acidocaldarius*

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In archaea, nothing is known about the β-alanine degradation pathway or its regulation. In this project, we have identified and characterized BarR, a novel Lrp-type transcription factor with a nonproteinogenic amino acid ligand. β-alanine is an important metabolite as it is the precursor of coenzyme A (CoA). Since the bacterial-type key enzymes in CoA metabolism are not conserved in archaea, the model archaeon *Sulfolobus* may have established a unique metabolic and regulatory pathway for β-alanine synthesis and degradation. BarR, conserved in *Sulfolobus acidocaldarius* and *Sulfolobus tokodaii*, is located in a divergent operon with a gene predicted to encode β-alanine aminotransferase. Deletion of *barR* resulted in a reduced exponential growth rate in the presence of β-alanine. Furthermore, qRT-PCR and promoter activity assays demonstrated that BarR activates the expression of the adjacent aminotransferase gene, but only upon β-alanine supplementation. In contrast, auto-activation proved to be β-alanine independent. The global binding profile of BarR, mapped with ChIP-seq, revealed additional *in vivo* binding sites. It was shown that BarR regulates a glutamine synthetase gene, thus connecting β-alanine with α-amino acid metabolism. Heterologously produced BarR protein behaves as an octamer in solution and forms a single complex by interacting with multiple sites in the 170 bp long intergenic region separating the divergently transcribed genes. *In vitro*, DNA binding is specifically responsive to β-alanine and site-mutant analyses indicated that β-alanine directly interacts with the ligand-binding pocket. Moreover, we have demonstrated that by using an archaeal BarR operator fused to a bacterial promoter, the regulator is capable of modulating gene expression in the bacterium *E. coli*, which is promising for the future development of a β-alanine inducible genetic circuit. In conclusion, this work contributes to the growing body of evidence that in archaea, Lrp-type transcription factors have physiological roles that go beyond the regulation of α-amino acid metabolism.