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Differential protein-DNA contacts for activation and repression by ArgP, a LysR-type (LTTR) transcriptional regulator in *Escherichia coli*.

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Abstract

ArgP is a LysR-type transcriptional regulator (LTTR) that operates with two effector molecules, lysine and arginine, to differentially regulate gene expression. Effector-free ArgP stimulates transcription of all investigated regulon members, except *argO*, whereas lysine abolishes this effect. Activation of *argO*, encoding an exporter for arginine and canavanine, is strictly dependent on arginine-bound ArgP. Lysine counteracts this effect and even though lysine-bound ArgP stimulates RNA polymerase recruitment at the *argO* promoter, the complex is non-productive. It is presently unclear what distinguishes *argO* from other ArgP targets and how binding of arginine and lysine translates in antagonistic effects on promoter activity. Here we generate high resolution contact maps of effector-free and effector-bound ArgP-DNA interactions and identify the sequence 5'-CTTAT as the consensus recognition motif for ArgP binding. *argO* is the only operator at which ArgP binding overlaps the -35 promoter element and binding of arginine results in a repositioning of the promoter proximal bound ArgP-arg subunits. This effect was mimicked by the generation of a 10 bp insertion mutant (*ins-10*) in the *argO* operator that renders its activation by ArgP arginine-independent. ArgP-induced DNA bending of the *argO* operator by approximately 60° was found to be effector independent. An ArgP:DNA binding stoichiometry of 4:1 indicates binding of four ArgP subunits even to DNA constructs that are truncated for one binding subsite (ΔABS). These results provide insight into the molecular mechanisms of ArgP-mediated regulation and a molecular explanation for the unique arginine-dependence of *argO* activation that distinguishes this particular ArgP target from all others.

Key words
IciA, *argO*, *lysP*, amino acid transport, DNA bending, DNA footprinting