ABSTRACT

The ArgP protein of *Escherichia coli* had previously been described variously by different investigators as an inhibitor of oriC-initiated DNA replication, a nucleoid-associated protein and as a transcriptional regulator of genes involved in DNA replication (*dnaA, nrdA*), osmoregulation and amino acid metabolism (*argO, dapB, gdhA* [the last in *Klebsiella pneumoniae*]). In the studies reported in this thesis, promoter-*lac* fusions were examined in argP*, ΔargP* and dominant argP (argP<sup>d</sup>) mutations bearing strains to identify additional ArgP-regulated genes. The genes *gdhA*, *lysP*, *lysC*, *lysA*, *dapD*, and *asd* were newly identified as ArgP-regulated. All were repressed upon Lysine (Lys) supplementation, and *in vitro* studies demonstrated that ArgP binds to the regulatory regions in a Lys-sensitive manner (in contrast to the behaviour at *argO*, where ArgP binding is Lys-insensitive). Unlike previous reports, neither *dnaA* nor *nrdA* was ArgP-regulated *in vivo*, although their regulatory regions did exhibit non-canonical low-affinity binding to ArgP *in vitro*.

ArgP-*argO* of *E. coli* and LysG-*lysE* of *Corynebacterium glutamicum* are orthologous regulator-target gene pairs. While LysE is an exporter of both arginine (Arg) and Lys whose expression is induced by Arg, Lys, or histidine (His), ArgO exports Arg alone and its expression is activated by Arg but not Lys or His. In studies reported in this thesis, reconstitution of LysG activation of *lysE* in *E. coli* was achieved. Neither ArgP nor LysG could regulate expression of the non-cognate targets, but the ArgP<sup>d</sup> variants -P274S, -S94L -P108S activated *lysE* expression in *E. coli*. The activating effects of LysG and ArgP<sup>d</sup> on *lysE* were mutually extinguished when both proteins were co-expressed in Arg- or His-supplemented cultures. Compared to native ArgP, these ArgP<sup>d</sup>s exhibited higher affinity of binding to *lysE* and less DNA bending at both *argO* and *lysE*. These findings represent the first example of transcriptional cross-regulation between a Gram-positive and Gram-negative bacterium.