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REVIEW

Quorum sensing in *Escherichia coli* and *Salmonella*

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Abstract

Quorum sensing in *Escherichia coli* and *Salmonella* has been an elusive topic for a long time. However, in the past 8 years, several research groups have demonstrated that these bacteria use several quorum-sensing systems, such as: the *luxS*/AI-2, AI-3/epinephrine/norepinephrine, indole, and the LuxR homolog SdiA to achieve intercellular signaling. The majority of these signaling systems are involved in interspecies communication, and the AI-3/epinephrine/norepinephrine signaling system is also involved in interkingdom communication. Both *E. coli* and *Salmonella* reside in the human intestine, which is the largest and most complex environment in the mammalian host. The observation that these bacteria evolved quorum-sensing systems primarily involved in interspecies communication may constitute an adaptation to this environment. The gastrointestinal tract harbors a high density and diversity of bacterial cells, with the majority of the flora residing in the colon (10^{11}–10^{12} bacterial cells/ml). Given the enormous number and diversity of bacteria inhabiting the gastrointestinal environment, it should not be surprising that the members of this community communicate amongst themselves and with the host itself to coordinate a variety of adaptive processes.

Keywords: *Escherichia coli*; *Salmonella*; Quorum sensing; AI-2; AI-3

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SdiA quorum-sensing system

Quorum sensing was first described in the regulation of bioluminescence in *Vibrio fischeri* (Nealson et al., 1970). The luciferase operon in *V. fischeri* is regulated by two proteins, LuxI, which is responsible for the production of the *N*-acyl-homoserine-lactone (AHL) autoinducer and LuxR, which is activated by this autoinducer to increase transcription of the luciferase operon (Engebrecht et al., 1983; Engebrecht and Silverman, 1984). Since this initial description, homologues of LuxR–LuxI have been identified in other bacteria and in all of these LuxR–LuxI systems, the bacteria produce an AHL autoinducer, which binds to the LuxR protein and regulates the transcription of several genes involved in a variety of phenotypes (Davies et al., 1998; de Kievit and Iglewski, 2000; Parsek and Greenberg, 2000). *Escherichia coli* and *Salmonella* have a LuxR homologue, SdiA (Wang et al., 1991), but do not have a *luxI* gene, and do not produce AHLs (Michael et al., 2001; Swift et al., 1999). The *E. coli sdiA* gene initially was isolated as a regulator of the cell division genes *ftsQAZ* (Wang et al., 1991). Although a cloned *sdiA* gene on a multi-copy plasmid can upregulate expression of *ftsQAZ* genes, an *sdiA* mutant has no apparent cell division defects (Wang et al., 1991). Kanamaru et al. (2000) found that expression of SdiA from a high-copy-number plasmid in enterohemorrhagic *E. coli* (EHEC) caused abnormal cell division, reduced adherence to cultured epithelial cells, and reduced expression of the intimin adhesin protein and the EspD protein, both of which are encoded on the locus of enterocyte effacement (LEE) pathogenicity island. However, no *sdiA* EHEC mutant was constructed and tested and so the effects seen could be artifacts due to the abnormally high expression of SdiA. Because no *E. coli* genes from either EHEC or K-12 have yet been demonstrated to be regulated by the single chromosomal copy of *sdiA*, Ahmer (2004) recently concluded that there are no confirmed members of a SdiA regulon in this species.

The precise role of SdiA in quorum sensing was elusive for several years until Michael et al. (2001) reported that SdiA is not sensing an autoinducer produced by *Salmonella* itself, but rather AHLs produced by other bacterial species. SdiA regulates a few genes in *Salmonella* including one gene potentially involved in resistance to human complement, *rck* (Ahmer et al., 1998). However, mutation of the *sdiA* gene had no effect on virulence of *Salmonella* in mouse, chicken or bovine models of disease (Ahmer, 2004).

Indole signaling

Indole is a diagnostic marker for the identification of *E. coli* and is formed from tryptophan by the tryptophanase enzyme, encoded by the *tna* gene. Wang et al. (2001) have demonstrated that indole can also act as a signaling molecule, and that it activates transcription of *gabT, astD* and *tnaAB* genes. Activation of the *tnaAB* operon is predicted to induce more indole production. The other two targets of indole-mediated signaling, *astD* and *gabT* are involved in pathways that degrade amino acids to pyruvate or succinate. These results led Wang et al. (2001) to speculate that signaling by indole may have a role in adaptation of bacterial cells to a nutrient-poor environment where amino acid catabolism is an important energy source.

The *luxS*/AI-2 quorum-sensing system

The most widespread quorum-sensing system is the *luxS* system, first described as being involved in bioluminescence in *Vibrio harveyi* (Surette et al., 1999). Among the diverse bacterial species that contain the *luxS* quorum-sensing system are *E. coli* and *Salmonella* (Surette and Bassler, 1998; Surette et al., 1999). LuxS is an enzyme involved in the metabolism of *S*-adenosyl-methionine (SAM); it converts *S*-ribosyl-homocysteine into homocysteine and 4,5-dihydroxy-2,3-pentanedione (DPD). DPD is a very unstable compound that reacts with water and cyclizes to form several different furanones (Schauder et al., 2001; Sperandio et al., 2003; Winzer et al., 2002a), one of which is thought to be the precursor of autoinducer-2 (AI-2) (Schauder et al., 2001). The AI-2 structure has been solved by co-crystallizing this ligand with its receptor LuxP (a periplasmic protein that resembles the ribose-binding protein RbsB) in *V. harveyi,* and reported to be a furanosyl-borate-diester (Chen et al., 2002). However, LuxP homologues, as well as homologues from this signaling cascade, have only been found in *Vibrio* sp. Many other bacterial genera harbor the *luxS* gene, and have AI-2 activity as measured using a *V. harveyi* bioluminescence assay (Schauder and Bassler, 2001; Xavier and Bassler, 2003). However, the only genes shown to be regulated by AI-2 in other species encode for an ABC transporter in *Salmonella typhimurium* named Lsr (LuxS-regulated), responsible for the AI-2 uptake (Taga et al., 2001). This ABC transporter is also present in *E. coli* and shares homology with sugar transporters. Once inside the cell, AI-2 is modified by phosphorylation and proposed to interact with LsrR, which is a SorC-like transcription factor involved in repressing expression of the *lsr* operon (Taga et al., 2001, 2003) (Fig. 1). Several groups have been unable to detect the furanosyl-borate-diester, proposed to be AI-2, in purified fractions containing AI-2 activity from *Salmonella* and *E. coli* sp. (as measured using the *V. harveyi* bioluminescence assay) (Schauder et al., 2001; Sperandio et al., 2003; Winzer