



Editorial: LuxR Solos are Becoming Major Players in Cell–Cell Communication in Bacteria

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Quorum sensing (QS) is the ability of microbes to sense and respond to their own population density, which typically results in cooperative activity (Fuqua et al., 1994). This form of microbial communication is important to agriculture and human health as they often participate in the regulation of genes important for host interactions.

The classic example of QS in bacteria is performed by the symbiotic bioluminescent bacterium *Vibrio fischeri* (Hastings and Greenberg, 1999). This bacterium colonizes the light organ of a squid and becomes luminescent at high population density. A pheromone of the acylhomoserine lactone class (AHL) is synthesized by the enzyme LuxI, and is a proxy for population density. The AHL is sensed by the transcription factor LuxR, which then activates the transcription of the *luxICDABEG* luciferase operon. Homologous LuxR-LuxI pairs have been found throughout the Proteobacteria (Fuqua et al., 2001); there is divergence among the structures of AHLs produced and detected by LuxI-LuxR pairs, providing some species specificity to the systems.

Several studies and the sequencing of many bacterial genomes has evidenced the presence of many AHL/QS-related *luxR*-type genes, which are unpaired to a cognate *luxI*. These LuxRs possess the typical modular structure having an AHL-binding domain and a DNA-binding HTH domain. These unpaired *luxRs*/LuxRs have been called orphans (Fuqua, 2006; Patankar and Gonzalez, 2009) and more recently solos (Subramoni and Venturi, 2009). Several questions arise on the role of LuxR solos in bacteria and recent studies have revealed a number of roles including eavesdropping, intra-species and inter-kingdom signaling. This research topic of *Frontiers in Cellular and Infection Microbiology* is a collection of 10 articles which highlight these different roles as well as the widespread distribution of LuxR solos.

Three articles highlight how widespread LuxR solos are and provide data on their phylogenetic distribution (Gan et al., 2014; Hudaiberdiev et al., 2015; Subramoni et al., 2015). These surveys have shown the presence of one or multiple predicted LuxR solos in many proteobacterial genomes living in different environments, some of them also harboring genes for one or more complete AHL-QS circuits. LuxR solos can be tentatively clustered into meaningful groups or putative orthologs. These LuxR solos subfamilies could respond to different signals and/or having different roles.

The functions of solos can thus far be sub-divided in four categories; as detecting endogenous or exogenous signals, of either the classical AHL type, or of a novel type. The AHL-responsive solos can firstly detect exogenous AHLs, i.e., AHLs synthesized by other organisms, and this category is typified by the LuxR solo, SdiA (Sperandio, 2010; Soares and Ahmer, 2011; Swearingen et al., 2013; Sabag-Daigle et al., 2015). Orthologs of *sdiA* are present in *Escherichia*, *Salmonella*, *Enterobacter*, *Citrobacter*, *Cronobacter*, *Klebsiella*, *Pantoea*, and *Erwinia* (Sabag-Daigle and Ahmer, 2012). The *Pantoea* and *Erwinia* orthologs are part of *luxR-luxI* pairs and represent the ancestral state, and the *luxI* homolog was lost in the remaining genera, giving rise to the *sdiA* solos (Sabag-Daigle and Ahmer, 2012). In this issue, an *sdiA*-regulon study is presented showing a number of genes

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regulated by SdiA in *Enterobacter cloacae* (Sabag-Daigle et al., 2015). Interestingly some target genes were regulated in the complete absence of AHLs and thus AHLs may not be a “folding-switch” for SdiA, in which SdiA only folds correctly in the presence of AHL (Yao et al., 2006; Nguyen et al., 2015), AHL may alter the DNA binding specificity of SdiA so that there are AHL-dependent and AHL-independent promoters. LuxR solos can also be used to detect endogenous AHLs, i.e., AHLs that are made by the species detecting them. This “third wheel” type of LuxR solo is typified by QscR of *Pseudomonas aeruginosa* which harbors two complete AHL QS circuits, namely LasI/R and RhII/R (Chugani and Greenberg, 2014; Martínez et al., 2015). In this issue, a review regarding the function of QscR is presented (Chugani and Greenberg, 2014; Martínez et al., 2015). QscR is involved in virulence and it responds to LasI generated AHLs, however it has a more relaxed specificity and is more promiscuous than LasR and its regulon overlaps with the one of LasR. The article particularly focuses on its biochemistry since QscR has become a model for understanding QS LuxR homologs.

LuxR solos can also respond to ligands which are not AHLs of either endogenous or exogenous sources. A large sub-family of LuxR solos has been found that specifically recognizes molecules from plants (González and Venturi, 2012; da Silva et al., 2015; Xu et al., 2015). These solos are only found in both pathogenic and beneficial plant-associated bacteria (PAB) and show changes in one or two highly conserved amino acids of the autoinducer binding domain (González and Venturi, 2012). Another member of this subfamily of PAB LuxR solos is reported in this *Frontiers*

topic (Xu et al., 2015) as well as studies of protein domain switching between these solos and classic AHL responsive motifs (da Silva et al., 2015). A major step forward will be to identify the class of plant molecules that these solos respond to. Some solos respond to an endogenous, non-AHL, ligand. The LuxR-type receptor PluR of *Photobacterium luminescens* responds to α -pyrones, while the related organism *Photobacterium asymbiotica* responds to dialkylresorcinols using the LuxR homolog PauR (Brachmann et al., 2013; Brameyer et al., 2014, 2015; Brameyer and Heermann, 2015; Chen et al., 2015). The synthases for these molecules were determined to be PpyS and DarABC, respectively. In this instance, the LuxR solos turned out not to be solo at all. Instead, these LuxR homologs are paired with previously unrecognized types of synthases. In this topic, a survey of these LuxRs in *Photobacterium* species is reported (Brameyer et al., 2014).

In summary, LuxR solos are widespread in Proteobacteria hence they are major players in bacterial communication and require more attention. Articles in this topic highlight the different modes of action of LuxR solos which are responding to endogenous and exogenous AHL or non-AHL signals. Further studies could lead to novel ways of controlling bacterial host colonization.

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