Strain-dependent diversity in the *Pseudomonas aeruginosa* quorum-sensing regulon

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**AUTHOR SUMMARY**

Bacteria use a means of chemical signaling called “quorum sensing” to control gene expression in response to cell density. Many Proteobacteria use acyl-homoserine lactones (AHLs) as signals for quorum-controlled regulation of ecologically and medically important traits. Species-dependent differences in quorum regulons have been well documented (1, 2). *Pseudomonas aeruginosa*, a bacterium occupying a range of environmental and clinical habitats, uses AHL signaling for gene regulation. Little is known about strain-dependent differences in the quorum response of *P. aeruginosa* or any other bacterial species. Recent technology advances in bacterial transcriptomics have made it possible to examine the quorum responses of isolates for which genomic sequence information previously was not available. We found that quorum responses of isolates from diverse habitats show differences that appear to reflect evolution under different ecological circumstances and their adaptation to specific niches.

The *P. aeruginosa* quorum-sensing system employs two distinct AHL-signaling molecules, 3OC12-HSL and C4-HSL, which are produced and sensed by the products of the las-lasR and rhl-rhlR gene pairs, respectively. We generated draft genomes for each of six strains and annotated each genome. We used a streamlined RNA-seq method to enrich for non-rRNA reads without the need for rRNA depletion to profile the transcriptomes of seven *P. aeruginosa* strains from diverse environmental and clinical habitats. We also created and analyzed quorum-sensing mutants of each strain.

The *las-lasR* and *rhl-rhlR* genes were conserved in each strain; however, our analyses show significant variation in the quorum responses of different *P. aeruginosa* strains. Within the confines of our study, the largest quorum regulon consists of 342 genes and belongs to a soil isolate; the smallest consists of 31 genes and belongs to a clinical isolate from a cystic fibrosis (CF) patient with a chronic lung infection. The quorum regulon of the reference laboratory strain PAO1 comprises 161 genes. Variations among strains are caused by differences in gene expression and differences in gene content.

Our genomic-sequence analysis is consistent with previous findings of a core set of genes conserved among the great majority of strains and accessory genes with a limited distribution among strains (3). Quorum-controlled genes were distributed among both the core and accessory genomes. For two strains, one isolated from soil and one from a tomato plant, we found examples in which an ecological basis can be inferred for traits regulated by strain-dependent quorum-controlled genes. Interestingly, these traits are encoded by genes of the accessory genome. Together, these findings suggest that in *P. aeruginosa* the evolution of quorum-sensing systems is a dynamic process influenced by ecological factors.

The two clinical isolates surveyed in this study are from different patients with chronic CF lung infections. Despite the seemingly similar nature of their niches, we found significant differences in their quorum regulons. One of the two clinical isolates has a significantly smaller quorum regulon and a generally tempered quorum response as compared with all other strains. It is interesting that several genes that are quorum controlled in other isolates (for example, the *hcn* operon encoding hydrogen cyanide synthase) are absent in one or both clinical isolates. Although our sample size is small, the relative incongruity between the regulons of the two CF isolates emphasizes the need for caution in drawing population-wide inferences for the *P. aeruginosa* quorum response for this environment. A case in point is the absence of genes encoding a functional hydrogen cyanide synthase in both CF isolates. This finding was not expected, because numerous previous studies have documented the production of cyanide by *P. aeruginosa* from the CF lung (4, 5).

Our analysis revealed 42 quorum-controlled genes in the majority of strains examined. We call these genes the “core quorum-controlled genes.” The analysis also revealed a larger set of strain-variable genes, including genes present on the accessory genome. Among the core set are genes for the production of public goods, secreted and excreted molecules that can be shared by community members. The strain-variable set includes genes encoding general metabolic enzymes, suggesting a link between quorum sensing and metabolic versatility. The strain-variable regulation of several environmentally responsive genes encoding known and putative transcription factors and two component signal-transduction systems suggests that *P. aeruginosa* coordinates quorum sensing with the differential integration of environmental signals.

The present study underscores the importance of probing multiple strains to understand the population-wide significance of quorum sensing for a species. It also provides a methodology and describes an analysis pipeline that makes possible largescale studies involving many more isolates than we have studied here. Specifically, our study of strain-dependent variation in *P. aeruginosa* indicates a broader role for quorum sensing in the ecology of *P. aeruginosa* that extends beyond its role in optimizing expression of public goods and virulence factors. Quorum-sensing circuits may be crucial for the ecological fitness of *P. aeruginosa* in diverse environments.


References 


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