

Emerging themes in bacterial cell-cell communication networks

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Bacteria use complex regulatory networks to adapt to their host and survive in changing environments. *Pseudomonas aeruginosa* can achieve this by integrating intracellular and intercellular signal switches with very intricate transcriptional and posttranscriptional mechanisms. This bacterium regulates the production of virulence determinants in a population-dependent manner via a hierarchical quorum sensing cascade involving two main regulatory circuits LasR/I and RhlR/I and their cognate activating signalling molecules, *N*-(3-oxododecanoyl)-L-homoserine lactone (3O-C12-HSL) and *N*-butanoyl-L-homoserine lactone (C4-HSL) respectively. *P. aeruginosa* also produces 2-heptyl-3-hydroxy-4(1*H*)-quinolone, the *Pseudomonas* quinolone signal (PQS) which biosynthesis and mode of action is modulated by the *las* and *rhl* systems. In addition, it possesses a very complex intracellular regulatory network driven by the secondary messenger c-di-GMP which plays a crucial role in both biofilm formation and motility in many bacterial species. We have found that some of the target genes controlled by these inter and intra-cellular signalling systems are also regulated by the Rsm global post-transcriptional regulatory system where the RsmA RNA-binding protein plays a key role. The global effects of RsmA are abrogated when transcription of the antagonist small non-coding RNAs RsmY and RsmZ is induced by the Gac two-component regulatory system which in turn is controlled by still unknown signals. We have shown that in *P. aeruginosa* there is a very tight relationship between quorum sensing, c-di-GMP signalling and the rsm posttranscriptional regulatory system to enable this organism to modulate, with great precision, key bacterial processes such as motility, biofilm formation and virulence factor production.