[S2-4]

Quorum Regulation of *Pseudomonas* Quinolone Signal (PQS) Biosynthesis in *Pseudomonas aeruginosa*

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Pseudomonas quinolone signal (PQS) plays a role in the regulation of virulence genes and it is intertwined in the *las*/*rhl* quorum sensing (QS) circuits of *Pseudomonas aeruginosa*. PQS is synthesized from a precursor, anthranilate by *pqsABCDE/phnAB* whose expression is influenced by the *las* and *rhl* systems. Since anthranilate can be also degraded into TCA cycle via catechol by functions of *antABC* and *catBCA* operons, the PQS synthesis from anthranilate should be regulated by the balance between the *pqsABCDE/phnAB* function and *antABC*/*catBCA* functions. Our real time PCR analyses showed that *antA* and *catA* are repressed by LasR until stationary phase and activated by the RhlR in late stationary phase in the same pattern, whereas *pqsA-E/phnAB* is activated by LasR in log phase and repressed by RhlR in opposite manner. QscR represses both functions but each repression on PQS synthesis function or anthranilate degradation function happened at different growth phase. Although this fine time-differential regulation is apparently accomplished by the antagonistic interplay of three QS regulators, LasR, RhlR, and QscR, it is not direct regulation of QS regulators. Instead, two intermediate regulators, AntR and PqsR directly regulate the *antA* and *pqsA* promoters in response to their cofactors, anthranilate and PQS, respectively, and then, the expressions of *antR* and *pqsR* genes are QS-regulated, where LasR activates *pqsR*, RhlR activates *antR* and represses *pqsR*, and QscR represses both *antR* and *pqsR* at different growth phase. While PQS production is positively regulated by LasR, the secretion of anthranilate at the late stationary phase was RhlR-dependent and PhnAB, anthranilate synthase that is activated by LasR was not responsible for the secretion. The *pqsA* activation was damped in stationary phase while the *pqsR* expression increased throughout growth, but introducing *rhlR* mutation extends the activation of *pqsA* into stationary phase, indicating that RhlR can post-transcriptionally inhibit PqsR. From these results, we suggest that RhlR and QscR negatively and time-differentially regulate PQS synthesis by affecting the expression and activity of AntR and PqsR reversely to what LasR does.