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phuR intergenic mutation results in pleiotropic effects on global gene expression

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We have previously found a positive selection for promoter mutations in *Pseudomonas aeruginosa* DK2 leading to increased expression of the *phu* (*Pseudomonas* heme utilization) system. By mimicking conditions of the CF airways *in vitro*, we experimentally demonstrated that increased expression of *phuR* confers a growth advantage in the presence of hemoglobin, thus suggesting that *P. aeruginosa* evolves towards iron acquisition from hemoglobin.

Further analysis of the effect of this promoter mutation in *P. aeruginosa* lead to discovery of new additional phenotypes such as enhanced inhibition of *Staphylococcus aureus* and a clear change in pigmentation of *P. aeruginosa* from white to green/yellow. To begin to understand the underlying mechanism of these pleiotropic effects, we performed Affymetrix GeneChip DNA microarray analysis on isogenic strains of *P. aeruginosa* DK2 with (M2) and without (WT) the *phuR* promoter mutations.

We find 163 gene expressions to be statistically different between the two strains, where the most significant difference was observed in the six local genes of the *phu* operon. Moreover, we see an apparent down-regulation of genes involved in other iron uptake system, possibly to compensate for the overexpression of the *phu* system. Interestingly, we find a number of stress related protein genes such as *ibpA*, *grpE* , *hscB*, *clpV1* and *clpX* to be up-regulated in M2 compared to WT. We therefore propose a model where significant overexpression of a membrane associated protein such as PhuR leads to a stress response that re-wires the transcription of certain genes. We are currently pursuing this model by further investigation of the target genes.