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Sodium hypochlorite affects biofilm formation, motility and c-di-GMP metabolism in *Pseudomonas aeruginosa*

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The opportunistic pathogen *Pseudomonas aeruginosa* is a versatile Gram-negative bacterium which is able to adapt to a variety of often harmful environmental conditions due to different survival strategies including regulation of gene expression and the formation of resistant biofilms. In this study we investigated the stress response of *P. aeruginosa* towards the disinfectant sodium hypochlorite (NaClO) which is frequently used in hospitals and drinking water treatment. In static biofilm assays we observed a significant increase in attachment after 2 hours of incubation with sublethal concentrations of NaClO as well as elevated biomasses of pregrown biofilms incubated with NaClO. Besides the significant upregulation of genes which are known to be involved in attachment and biofilm formation, microarray analyses of chlorine treated cells compared to untreated controls revealed an enhanced expression of ORF PA3177 coding for a putative di-guanylate-cyclase. These enzymes catalyze the synthesis of the second messenger c-di-GMP which considerably influences motility, biofilm formation and persistence in *P. aeruginosa*. Subsequent LC-MS/MS analyses of bacterial lysates showed indeed a significant increase in c-di-GMP levels in response to chlorine treatment suggesting a key role of this second messenger in hypochlorite induced biofilm formation. Moreover, PA3177 overexpression in *P. aeruginosa* resulted in increased attachment, impaired motility and elevated intracellular c-di-GMP levels. The function of PA3177 in the stress response of *P. aeruginosa* towards biocides was further investigated in more detail by mutant screening and qRT-PCR in order to identify potential regulators of PA3177 gene expression.