We found that thiourea substantially promotes extinction of evolving bacterial populations for all three cases of bactericid antibiotics treatments both in the case of mutators and non-mutators. Our results indicate that scavenging of reactive oxygen species by thiourea substantially reduces mutational input, and hence the corresponding populations had lower opportunity to evolve resistance against the used antibiotic. Thiourea treatment had no significant impact on extinction rates of the populations adapted to the bacteriostatic drug trimethoprim. We found that the impact of ROS formation on resistance evolution is at least partially independent of the SOS response. Our work suggests that enhancement of ROS formation may be useful for improving antibiotics lethality in the short term, but it also accelerates drug resistance evolution.

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Investigation of a novel stress-induced operon in *Synechocystis* PCC 6803

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Cyanobacteria are photosynthetic prokaryotes that are widely used model organisms of photosynthetic research according to their close relationship to chloroplasts. These prokaryotes possess a variety of adaptation mechanism by which they are able to inhabit different extreme biotops. Since they are autotrophic organisms they are the primary producers of these niches. Among others, arsenic compounds and hydrogen sulfide are widely distributed in nature since the origin of life. Cyanobacteria have evolved mechanisms to cope with the toxicity of these substances. In order to maintain their homeostasis under fluctuating environmental changes cyanobacteria evolved environmentally inducible detoxification systems.

We investigated the expression pattern of different genes upon heavy metal treatment in *Synechocystis* sp. PCC 6803 and discovered a novel gene cluster that responds to As^{3+}. This operon is located on the pSYSM plasmid and contains four genes, termed *artRSCT*. *ArtR* and *artS* are transcribed in the opposite direction of that of *artC* and *artT*, with a common promoter region between these two tandem gene pairs.

The gene product of *artR* shows high homology with DNA-binding proteins of the ArsR family. We have constructed a deletion mutant in order to inactivate the *artR* gene. In this mutant we observed high constitutive expression of the *artS/C/T* genes using quantitative RT-PCR technique. This fact supported our hypothesis that it functions as a common repressor of the genes. We have cloned and expressed this protein in *E. coli* in order to obtain further proof of its function. Using this purified protein we performed an electrophoretic mobility shift assay, which confirmed the specifity of ArtR towards the promoter sequence. Taken all these results into consideration we have proven that the protein product of *artR* is a regulator of the *artRSCT* operon, which binds to the common promoter and dissociates in the presence of As^{3+}.

ArtT shows high homology with membrane-bound heavy metal transporter proteins and because it is induced by As^{3+}, we assumed that it may be part of an arsenic resistance system. In order to test this hypothesis we have constructed an *artT* insertional mutant. The results were contradictory to our hypothesis because the mutant was more resistant to elevated amounts of As^{3+} then the wild type. Thus the function of *artT* may be different from that of the arsenic resistance genes.

The protein product of *artS* gene is homologous to sulfide-quinone oxido-reductases (SQR) and shows a high expression not only to As^{3+} but to Na_2S as well. Moreover *Synechocystis* PCC 6803 was more resistant to high amounts of Na_2S then other cyanobacterial species that lacks the SQR enzyme.

H_2S and As^{3+} can serve as alternative electron donors in many ancient anaerobic photosynthetic systems. The procaryotes capable of this type of electron transport use a single photosystem (PSI) and harbor a SQR enzymes, which oxidize sulfide to sulfur. Other strains can use arsenite oxidase enzyme to grow phototrophically in As^{3+} containing anaerobic environment. The facts that the *artRSCT* genes are induced by As^{3+} and Na_2S and the strain is more tolerant to Na_2S, than those which lack such genes suggest that these genes, especially *artS* may be involved in sulfide tolerance or sulfide metabolism of the cyanobacterium.

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