CONCERTED RESPONSES TO IRON AVAILABILITY IN CYANOBACTERIA

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Cyanobacteria are believed to be the first organisms to perform oxygenic photosynthesis. They have successfully conquered most of the environmental conditions on Earth. Their living habitats range from soil and freshwater to the open sea; and they contribute to a significant proportion of the CO_2 fixation, thus to the global biomass production. Beside their ecological importance, their capacity for adaptation has made the discovery of the underlying molecular networks a fascinating field of research.

An intriguing example for this adaptive capacity is given by iron homeostasis. Iron is an essential cofactor in many metabolic reactions, being a limiting factor for aquatic organisms due to its insolubility in the presence of oxygen. At the same time, due to its toxicity the concentration of intracellular iron must be under strict control. Therefore, the mechanisms controlling its homeostasis have to be coordinated with not only the extracellular conditions but also the general cellular state. Such coordination requires mechanisms on different time scales. Small RNAs, e.g. ryhB, have been shown to be crucial for fast responses while slower responses depend on modulation of transcription factors such as the ferric uptake regulator (Fur). This complex behavior needs to be approached by methods of in vivo, in vitro and in silico biology. Such an approach is presented here.

As model systems, we have used *Synechocystis* sp. PCC6803 due to the availability of relevant Fur mutants as well as of genome-wide expression data. As a first step, we have collected publically available microarray data for conditions of iron limitation and excess. In total, 21 microarrays from 5 experiments and 3 technical platforms were integrated. Here, we could detect a notable influence of the experimental platform indicating that results from a single platform should be treated with caution. Nevertheless, a conserved set of genes was found to be differentially expressed (logFC > 1.4 and an adjusted P value < 0.05) in all analysed experiments. Furthermore, clustering analysis demonstrated the tight control existing between photosynthesis related genes and iron availability. This was further explored by functional analysis which showed that expression of genes coding for photosynthesis and transport related proteins were the most affected by the iron concentration.

Complementary to genome-wide analyses, a core regulatory network for iron homeostasis was constructed in silico employing existing knowledge on iron homeostasis in *E. coli*. The integration of the constructed regulatory network and the collected expression data gave us a first dynamic model of the molecular adaption of *Synechocystis* to changes in external iron concentration.