**Understanding $CO_2$ uptake and proton pumping in cyanobacterial Photosynthetic Complex 1.**

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To survive under low $CO_2$ concentrations, cyanobacteria have evolved unique mechanisms that enhance the efficiency of photosynthetic $CO_2$ fixation. The $CO_2$ Concentrating Mechanism (CCM) in cyanobacteria includes specialized NADPH Dehydrogenase Type I complexes (a.k.a. Photosynthetic Complex-1 or PC1 or NDH-1 complexes) whose major function is to provide enough inorganic carbon (Ci) to Rubisco in low Ci conditions. These complexes possess extrinsic subunits specially evolved for high or low affinity $CO_2$-uptake, CupA and CupB respectively. The catalytic site at the interface between the extrinsic CupB and transmembrane NdhF4 subunits of the $CO_2$ uptake module of these complexes differs from regular carbonic anhydrases because of their unusual Zinc coordination. This Zn in the putative $CO_2$ binding site is coordinated by residues from the neighboring NdhF4 subunit; namely Arg37 and Tyr41 residues. We hypothesize that Arg37 around the active site of the Cup proteins in the NdhF4 subunit plays an important role in mediating the pumping of protons away from the $CO_2$ hydration active site. To test this, we generated R37 mutants and examined their growth phenotypes and carbonic anhydrase activities. Our results show that mutants exhibit severe growth defects under low Ci supporting a direct role for Arg37 in moving the generated proton away from the active site fast enough for the $CO_2$ hydration reaction to proceed unidirectionally and in an energized manner, preventing the reverse reaction back to $CO_2$.

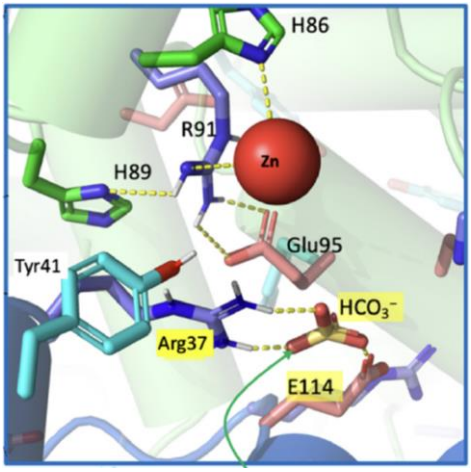


**Figure1.** The active site of the $CO_2$ concentrating CupB subunit, showing Zn-coordinating residues.

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