OA3.5 - Structural basis of Calvin cycle regulation by CP12

James W. Murray[1], Ciaran R. McFarlane[1], Nita Shah[1], Burak V. Kabasakal[1], Charles A.R. Cotton[1], Doryen Bubeck[1]

[1] Dept. Life Sciences, Imperial College, Exhibition Road, London, SW7 2AZ, UK

The Calvin cycle is regulated in response to the activity of the light-reactions. One mechanism for regulation is via the redox-sensitive protein CP12. CP12 is a small (~10 kDa) largely disordered protein found in almost all green-type phototrophs. In the dark, two disulfide bridges form, causing CP12 to transition to an ordered conformation. CP12 then forms an inhibited enzyme complex with glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and phosphoribulokinase (PRK). GAPDH is the reductive step after carboxylation by Rubisco. PRK is the step prior to Rubisco, making the substrate, ribulose-1,5-bisphosphate. Co-inhibition of GAPDH and PRK shuts down carbon fixation, by stopping flux through the Calvin cycle at two points before and after Rubisco, saving ATP, NADPH and Calvin cycle intermediates.
We used CP12 as bait to pull down GAPDH and PRK from a cyanobacterium, showing that the ternay complex exists in cyanobacteria as well as higher plants. We have solved the crystal structure of full-length CP12 bound to GAPDH, which sheds light on the disorder to order transition in CP12, and the effect of NAD vs NADP on complex formation. We have solved by cryo-electron microscopy the structure of the GAPDH-CP12-PRK complex and built an atomic model. This gives us a view of green-type PRK, and the mechanism of inhibition by its own disulfide bonds and the N-terminal domain of CP12. We can also see how GAPDH and PRK interact in the complex, and the ordered oxidized structure of CP12.
The structure of the cyanobacterial complex is directly relevant to the equivalent chloroplast complex, and has implications for understanding and then manipulating the redox regulation of the Calvin cycle.
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