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# Unravelling the regulation pathway of photosynthetic AB-GAPDH

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Photosynthetic glyceraldehyde 3-phosphate dehydrogenase (GAPDH) is a key enzyme of the Calvin-Benson cycle. In higher plants different photosynthetic GAPDHs exist: the most abundant is formed by heterotetramers of A and B-subunits (AB-GAPDH). Being the major consumer of photosynthetic NADPH the enzyme is strictly regulated. The AB-GAPDH is indeed able to turn off its activity through oligomerization, a self assembly process mediated by the redox-sensitive B subunits tail called C-terminal extension (CTE). Typically, the fully inactive form is considered an hexadecamer A8B8, generated by the assembly of four A2B2-GAPDH tetramers [1].
Our combined small angle x-ray scattering coupled with size exclusion chromatography (SEC-SAXS) and cryo-electron microscopy (cryo-EM) analysis revealed the presence of several AB-GAPDH oligomers [(A2B2)n-GAPDH oligomers with n=1, 2, 4 and 5] co-existing in a dynamic system and dependent on the solution conditions (activation/inactivation). We observed a great, and only partially explored, compositional and conformational heterogeneity that prevented us to obtain high resolution structures of AB-GAPDH oligomers (Fig. 1 A, B). The resolution we achieved was high enough to understand the inactivation/oligomerization mechanism common to all observed AB-GAPDH oligomers. The oligomerization was indeed obtained by the mutual exchange among adjacent B-subunits of their CTEs, which act as protruding hooks that dock into the active sites of adjacent subunits substantially blocking the access of the substrate.

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