Cryo-EM Structures of Photosystem I with Alternative Quinones Reveals New Insight into Cofactor Selectivity

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Photosystem I (PSI) is a key protein involved in oxygenic photosynthesis. It is a multi-subunit membrane bound protein complex which performs light capture and electron transfer reactions, whose investigation has a rich history. In cyanobacteria, PSI is a "trimeric" protein complex with each monomer containing 10 to 12 protein subunits and many cofactors, 11 of which form its electron transfer chain. The electron transfer chain of PSI is split into two branches, and a key component of each branch is the phylloquinone (PhQ) that is involved as a permanently bound electron transfer intermediate. Previous data suggested that in the mutant cyanobacterial strain Δ*menB Synechocystis* sp. PCC 6803, which contains a mutation interrupting PhQ synthesis, each quinone site in PSI was instead occupied by plastoquinone-9 (PQ9), which is the native quinone found in PSII, and that PQ9 could be readily exchanged for alternative quinones. This model has since been used for many biophysical studies on electron transfer in PSI, but limited structural data is available to aide reliable interpretation. Here, we present two new cryo-EM structures of PSI containing alternative quinones: one in which PSI contains PQ9, and one in which the PQ9 has been exchanged in vitro for ethyl-naphthoquinone. These structures provide new insights into the selectivity of quinones in PSI, the stability conferred by central cofactors, and new evidence towards understanding the evolutionary ancestry of PSI. This investigation advances efforts to develop precisely engineered PSI-based systems for light-driven hydrogen production, offering a pathway toward sustainable alternatives to fossil fuels.

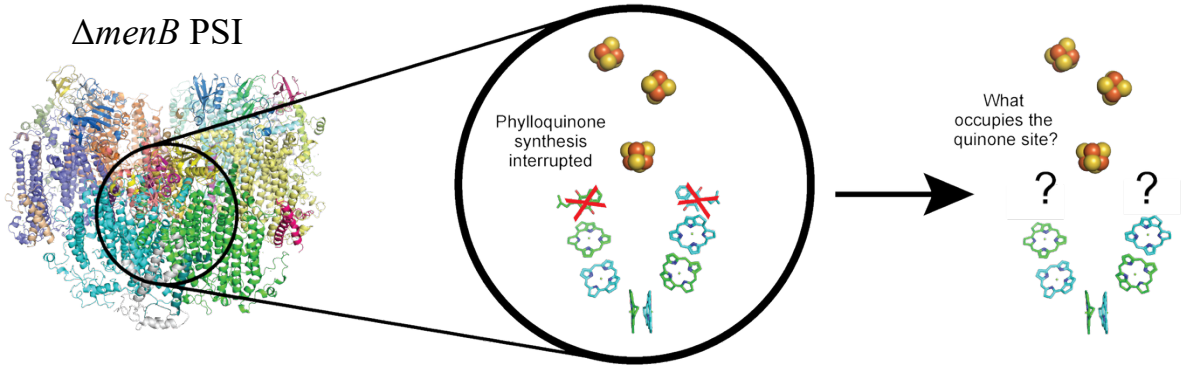

Figure. 1. The Δ*menB* mutant inhibits phylloquinone (PhQ) synthesis, a cofactor typically bound by PSI. We utilized cryo-EM structures of PSI from a newly generated Δ*menB* strain ("Δ*menB*"), and of that same PSI after EtNQ exchange ("Δ*menB*+EtNQ") to determine which quinones occupy the two quinone binding sites within each PSI monomeric unit.