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ACCEPTED MANUSCRIPT

Selenophosphate synthetase 1 and its role in redox homeostasis, defense and proliferation

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Abstract

Selenophosphate synthetase (SEPHS) synthesizes selenophosphate, the active selenium donor, using ATP and selenide as substrates. SEPHS was initially identified and isolated from bacteria and has been characterized in many eukaryotes and archaea. Two SEPHS paralogues, SEPHS1 and SEPHS2, occur in various eukaryotes, while prokaryotes and archaea have only one form of SEPHS. Between the two isoforms in eukaryotes, only SEPHS2 shows catalytic activity during selenophosphate synthesis. Although SEPHS1 does not contain any significant selenophosphate synthesis activity, it has been reported to play an essential role in regulating cellular physiology. Prokaryotic SEPHS contains a cysteine or selenocysteine (Sec) at the catalytic domain. However, in eukaryotes, SEPHS1 contains other amino acids such as Thr, Arg, Gly, or Leu at the catalytic domain, and SEPHS2 contains only a Sec. Sequence comparisons, crystal structure analyses, and ATP hydrolysis assays suggest that selenophosphate synthesis occurs in two steps. In the first step, ATP is hydrolyzed to produce ADP and gamma-phosphate. In the second step, ADP is further hydrolyzed and selenophosphate is produced using gamma-phosphate and selenide. Both SEPHS1

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