**Crystal Structure of 5-Aminolevulinate Synthase of *Rhodobacter capsulatus***

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5-Aminolevulinate synthase (ALAS) is the first and rate-limiting enzyme of heme biosynthesis in humans, animals, other non-plant eukaryotes and α-proteobacteria. It catalyzes the synthesis of 5-aminolevulinic acid, the first common precursor of all tetrapyrroles, from glycine and succinyl-coenzyme A.

eALAS (e for erythroid) is one of two isoforms of ALAS expressed in mammals and is responsible for approximately 90 % of body heme production. Naturally occurring mutations in human eALAS directly cause a hereditary disease known as X-linked sideroblastic anemia (XLSA). These disorders are characterized by inadequate formation of heme and accumulation of iron in erythroblast mitochondria.

We solved the crystal structure of ALAS of *Rhodobacter capsulatus*, 50 % identical by sequence to its human counterpart, at a resolution of 2.1 Å. Additional structures with each of the substrates glycine and succinyl-CoA reveal the active site organization and provide new insight into the enzyme mechanism.

We can now locate most naturally occurring XLSA mutations with high precision and interpret the clinical XLSA-cases in terms of the three-dimensional structure of the enzyme involved. Thus new impetus is given to finding ways of treating XLSA.

In addition the structure of ALAS completes the structural analysis of enzymes in heme biosynthesis.

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