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Distortion of porphyrin substrate in ferrochelatase catalysis

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Ferrochelatase catalyzes the terminal step of the heme biosynthetic pathway by inserting ferrous iron into protoporphyrin IX [1,2]. Porphyrin binding to murine ferrochelatase, the terminal enzyme of the heme biosynthetic pathway, was investigated employing a set of variants harboring mutations in a putative porphyrin-binding loop [3]. Using resonance Raman (RR) spectroscopy, the structural properties of the ferrochelatase-bound porphyrins were examined, especially with respect to the porphyrin deformation occurring in the environment of the active site. This deformation of the porphyrin substrate has been proposed to be a key step in the enzymatic insertion of ferrous iron into the porphyrin ring to yield heme [1,2]. Our results indicate that the degree of a specific non-planar porphyrin deformation contributes to the catalytic efficiency of ferrochelatase and its variants. Porphyrin binding to the ferrochelatase variants causes a decrease in the intensity of the RR out-of-plane vibrational mode γ_{15}, a saddling-like mode that is strong in the wild-type enzyme. In particular, the variant with catalytic efficiency one order of magnitude lower than that of wild-type enzyme is estimated to produce less than 30% of the wild-type saddling deformation.

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