Poster Presentation

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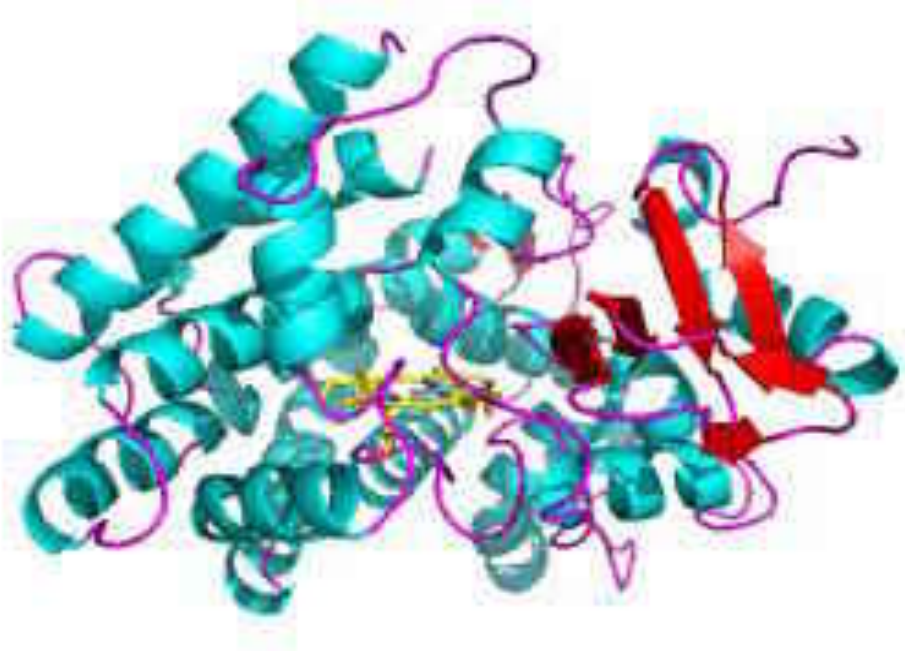
The crystal structure of the cytochrome P450 enzyme TxtE

F. Yu[1], M. Li[1], C. Xu[1], Z. Wang[1], H. Zhou[1], M. Yang[1], Y. Chen[1], J. He[1]

[1]*Shanghai Institute of Applied Physics, Chinese Academy of Sciences, Shanghai, China*

Thaxtomins, a family of phytotoxins produced by Streptomyces spp., can causes plant cell necrosis at nanomolar concentrations. Thaxtomin A is the dominant form from Streptomyces scabies and has demonstrated herbicidal action. TxtE, a cytochrome P450 enzyme from S. scabies 87.22, catalyzes direct nitration of the indolyl moiety of L-tryptophan to L-4-nitrotryptophan using nitric oxide, dioxygen and NADPH, which is the key step of Thaxtomin A biosynthesis. NO-related nitration is a common chemical process in organisms, particularly for tyrosine nitration. However, TxtE is the first reported enzyme that catalyzes a direct nitration reaction specifically in a biosynthetic pathway and thus it can potentially be developed for industrial applications. The crystal structure of TxtE was determined at 2.1 angstrom. A clearly defined substrate access channel is observed and can be classified as channel 2a, which is common in bacteria cytochrome P450 enzymes. A continuous hydrogen bond chain from the active site to the external solvent is observed. Compared with other cytochrome P450 enzymes, TxtE shows a unique proton transfer pathway which crosses the helix I distortion. Polar contacts of Arg59, Tyr89, Asn293, Thr296, and Glu394 with L-tryptophan are seen using molecular docking analysis, which are potentially important for substrate recognition and binding. After mutating Arg59, Asn293, Thr296 or Glu394 to leucine, the substrate binding ability of TxtE was lost or decreased significantly. According to docking and mutagenesis experiments, we propose a possible substrate recognition and binding mechanism, a possible mechanism for substrate recognition and binding is proposed.



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