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The Structure of NTBC Bound to 4-Hydroxyphenylpyruvate Dioxygenase. June M. Brownlee, Kayunta Johnson-Winters, David H. T. Harrison, Graham R. Moran, UW-Milwaukee, Milwaukee, WI, Rosalind Franklin Univ. of Medicine & Science, North Chicago, IL.

4-Hydroxyphenylpyruvate dioxygenase (HPPD) is involved in the catabolic pathway of tyrosine, taking the substrate to homogentisate. In plants it is the target of natural and synthetic herbicides. In humans, type I tyrosinemia patients fair significantly better when given an HPPD inhibitor. Orthorhombic crystals of recombinant Fe(II) HPPD from *Streptomyces avermitilis* complexed to the drug/herbicide 2-[2-nitro-4-(trifluoromethyl)benzoyl]-cyclohexanedione (NTBC) were found to have two molecules in the asymmetric unit and diffract to a resolution of 2.5 Å using synchrotron radiation. MR using the distantly related Fe(III) structure of HPPD from the *Pseudomonas fluorescens* failed to give a satisfactory solution. Single wavelength data collected at the Fe anomalous peak was used to determine the structure by the SAD method with the programs SOLVE/RESOLVE. The structure reveals sizeable shifts in a b-hairpin and the terminal a-helix near the active site, as well as other subtle changes.

This is the first structure of an HPPD-inhibitor complex to be determined. The stability of the Fe(II) form of the enzyme bound to NTBC has been demonstrated in vitro, and the electron density clearly shows the presence of NTBC in the active site.