Abstract

L-amino acid oxidase from *Rhodococcus opacus* is classified as a member of the GH_2-family of flavin-dependent oxidoreductases according to a highly conserved sequence motif. The protein contains non-covalently bound FAD in the elongated form. LAAO catalyzes the stereospecific oxidative deamination of an L-amino acid substrate to the corresponding α-keto acid along with the production of ammonia und hydrogenperoxide via an imino acid intermediate. With no homologous structure known the structure was solved *de novo* from anomalous differences of a mercury derivative using the SAD-technique.

The bacterial LAAO forms a homodimer with an unusual huge contact area. This mode of dimerization is not known for other members of the GH2-family so far. The monomer consists of three well-defined domains: the FAD-binding domain corresponding to a general topology throughout the GH2-family; a substrate-binding domain with almost the same topology than the snake venom LAAO and a helical domain exclusively responsible for the unusual dimerization mode of the protein and not found in other members of the family.

The high-resolution structures of the unbound protein as well as two substrate and one inhibitor complex compared to the structure of snake venom LAAO and DAAO from yeast and pig kidney give insight into the mode of reaction of this enzymes. Reduction of the flavin leads to an imino acid intermediate using a hydrid transfer mechanism. This mechanism appears to be uncommon in that the chemical transformation can proceed efficiently without the involvement of amino acid functional groups. Most groups present at the active side are involved in substrate recognition, binding and fixation, i.e. they direct the trajectory of the interacting orbitals. In this mode of catalysis orbital steering/interactions are the predominant factors for the chemical step(s).