

X-ray structures and catalytic mechanism of Urate Oxidase

Mohamed Chiadmi^a, Laure Gabison^a, Nathalie Colloc'h^b, Thierry Prangé^a

^a *Laboratoire de cristallographie et RMN biologique (UMR8015 CNRS), faculté de Pharmacie, Université René Descartes, 4 avenue de l'observatoire, 75270 Paris Cedex 06, France*

^b *UMR 6185 CNRS, Université de Caen, Centre Cyceron, Bd Becquerel, BP 5229, 14074 Caen Cedex, France*

Urate oxidase belongs to the purine degradation pathway and catalyzes, in the presence of molecular oxygen the hydroxylation of uric acid to a metastable product identified as the 5-hydroxyisourate (5-HIU). Once released in solution, 5-HIU decays slowly to allantoin, a process independent of oxygen and associated with the production of CO₂ (dehydro-decarboxylation). In vivo, 5-HIU is completely processed to [S]-allantoin by two specific enzymes, Hydroxyisourate Hydrolase and OHCU-decarboxylase.

The catalytic mechanism of urate oxidase is original since it does not imply any cofactor or metal ion, questioning about how urate, a singlet, can react with oxygen, a triplet. Several X-ray structures with uric acid and its analogues have been determined to unravel the three-dimensional active site topology. Complex Structures using pure oxygen under high pressure, uric acid in absence of oxygen and uric acid with cyanide gave information about the first step of the reaction, showing the natural substrate binding and pointing out a common site where successively O₂ and an essential H₂O partners proceed. The catalytic mechanism of this cofactor-less enzyme will be discussed at the light of these results.