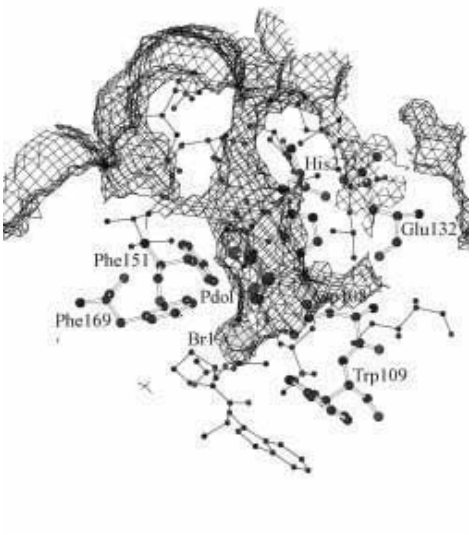
**s8a.m1.p21** **Crystal structure of the haloalkane dehalogenase from *Sphingomonas paucimobilis* UT26.** J. Marek[1], J. Vévodová[1], I. Kutá-Smatanová[1], Y. Nagata[2], L.A. Sven-sson[3], J. Newman[4], M. Takagi[2] & J. Damborsky[1]. [1]*Faculty of Science, Masaryk University, Kotlárská 2, CZ 611 37 Brno, Czech Republic.* [2]*University of Tokyo, Yayoi, Bunkyo-ku, Tokio 113-8657, Japan.* [3]*Department of Molecular Biophysics, Lund University, S-221 00 Lund, Sweden.* [4]*Structural GenomiX, 10505 Roselle St., San Diego, CA 92121, USA.*
Keywords: haloalkane dehalogenase, hexachlorocyclo-hexane, alpha/beta hydrolase.

The haloalkane dehalogenase from *Sphingomonas paucimobilis* UT26 (LinB) is the enzyme involved in the degradation of important environmental pollutant γ-hexachlorocyclohexane. The enzyme hydrolyses broad range of halogenated cyclic and aliphatic compounds. Here, we present the 1.58 Å crystal structure of LinB and 2.0 Å structure of LinB with 1,3-propanediol, a product of debromination of 1,3-dibromopropane, in the active site of the enzyme. The enzyme is α/β hydrolase and contains a catalytic triad (Asp108, His272 and Glu132) in the lipase-like topological arrangement previously proposed from mutagenesis experiments. The LinB structure was compared with the structures of haloalkane dehalogenase from *Xanthobacter autotrop-hicus* GJ10[1] and from *Rhodococcus* sp. [2] and the structural features involved in the adaptation towards xenobiotic substrates were identified. Arrangement and composition of the α-helices in the cap domain resulting in the differences in the size and shape of the active site cavity and the entrance tunnel (see VOIDOO representation of the active site cavity at fig) are the major determinats of the substrate specificity of the haloalkane dehalogenases.




[1] Franken, S. M., Rozeboom, H. J., Kalk, K. H. & Dijkstra, B. W. "Crystal structure of haloalkane dehalogenase: an enzyme to detoxify halogenated alkanes.", *EMBO J.,* (1991), **10**,1297-1302.
[2] Newman, J. *et al.* "Haloalkane Dehalogenases: Structure of a *Rhodococcus* Enzyme.", *Biochemistry,* (1999), **38**, 16105-16114.

**s8a.m1.p22** **Crystal structure of aldehyde reductase from *Sporobolomyces salmonicolor.*** A. Kita[1], M. Kataoka[2], K. Tanimizu[1], H. Kawabata[2], S. Shimizu[2] and K. Miki[1,3]. [1] *Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto 606-8502, Japan,* [2]*Department of Agricultural Chemistry, Graduate School of Agriculture, Kyoto University, Sakyo-ku, Kyoto 606-8502, Japan,* [3]*RIKEN Harima Insititute/SPring-8, Hyogo 679-5148, Japan.*
Keywords: crystal structure, NADPH-dependent aldehyde reductase, red yeast.

Aldehyde reductase, a member of the aldo-keto reductase superfamily, is a monomeric enzyme that catalyzes the NADPH-dependent reduction of a variety of aldehydes to their corresponding alcohols. This enzyme is a target for drug design because of its implication in diabetic complications. We have determined the crystal structures of aldehyde reductase from a red yeast, *Sporobolomyces salmonicolor* (apo-AR), and its complex with NADPH (holo-AR). Crystals of apo- and holo-AR were obtained from ammonium sulfate and PEG 4K solutions, respectively [1]. The both structures were solved by the molecular replacement method. The crystallographic R factors after refinements are 0.21 at 1.7 Å resolution and 0.21 at 1.8 Å resolution for apo- and holo-AR, respectively. The structure shows that the entire folding of AR is similar to those of the other aldehyde reductases or aldose reductases. AR consists of an alpha/beta (TIM) barrel and the active site is located at the carbonyl terminus of strands of the barrel. However, the folding pattern of the C-terminal region which includes a specific disulfide bond is much different from those of the other family. The NADPH is bound in an extended conformation with the adenine ring at the periphery and with the nicotinamide moiety forming a part of the basement of the active pocket. Most of residues essential for binding NADPH in AR are conserved in aldo-keto reductase superfamily, but the residue corresponding to Trp220 of human aldehyde reductase is missing. A comparison of apo-and holo-AR suggests that the binding of AR to NADPH requires significant conformational changes in AR. The side chain of Trp20 in active site changes its position to accommodate the cofactor. In addition, side chains of Lys256 and Arg262 undergo conformational changes up on the NADPH binding to form salt bridges with the adenine-2'-phospate moiety. Because AR does not make a complex with NAD, the conformational changes in the residues interacting with the adenine-2'-phospate moiety might be important to keep the tight binding with NADPH.

[1] M. Kataoka, et al., "Crystallization and preliminary X-ray diffraction study of aldehyde reductase from a red yeast, Sporobolomyces salmonicolor." Acta Cryst., (1996), D52: 405-406