BL-5A/2014G502, 2015G001

Crystal structure of NAD(P)H-dependent carbonyl reductase specifically expressed in the thyroidectomized chicken fatty liver

Kazunari Yoneda*[1], Yudai Fukuda[1], Takeki Sone[1], Haruhiko Sakuraba[2] and Toshihisa Ohshima[3]

[1]Department of Bioscience, School of Agriculture, Tokai University, Aso, Kumamoto, Japan
[2]Department of Applied Biological Science, Faculty of Agriculture, Kagawa University, 2393 Ikenobe, Miki-cho, Kita-gun, Kagawa, 761-0795, Japan
[3] Department of Biomedical Engineering, Osaka Institute of Technology, Osaka, Japan

1 Introduction

The functionally unknown 29 kDa protein which specifically expressed in thyroidectomized (Tx) chicken fatty liver have been reported. On the basis of genome information of the chicken (*Gallus gallus*), we recently identified the gene encoding the protein. From comparison of the amino-acid sequence of this protein with those of the homologues whose crystal structures have been determined to date, we found that the protein exhibits the highest identity (36%) with a CR from fruit-fly *Drosophila melanogaster* (PDB entry 1sny) and contains the two consensus sequences (S-Y*XXX*K, G*XXX*G*X*G) of the SDR family. Moreover, we succeeded in the expression of the gene in *E. coli* and confirmed that the gene product surely exhibits CR activity [1]. Since the enzyme shows rather low sequence identities with CRs from human (33%), mouse (30%), and pig (27%), it is of interest to examine structural differences among insect, chicken, and mammalian CRs. The physiological function of the CR in Tx chicken fatty liver is currently unknown. The enzyme probably contribute to metabolism of accumulated ketone body derived from fatty acid. Structural analysis of the enzyme may provide important information about its physiological substrate and function.

In this study, we determined the crystal structure of this enzyme at 1.98 Å resolution in the presence of NADPH and substrate analogue, ethylene glycol [2].

2 Experiment

Single-wavelength (1.0 Å) data for Tx chicken fatty liver CR was collected on the beamline 5A at the Photon Factory. The data were processed using HKL2000 and the CCP4 program suite.

3 Results and Discussion

The structure of the NADPH-bound Tx chicken fatty liver CR was determined using MR and was refined at a resolution of 1.98 Å to a crystallographic *R*-factor of 20.1% and a free *R*-factor of 21.1%. The asymmetric unit consisted of one dimer with a solvent content of 51.7%, which corresponds to a Matthew's coefficient of 2.57 $Å^3Da^{-1}$. The final model was comprised of amino acid residues -9 to 259 (A chain), 4 to 259 (B chain), two NADPH coemzymes, two ethylene glycol molecules and 229 waters (Fig. 1, 2).

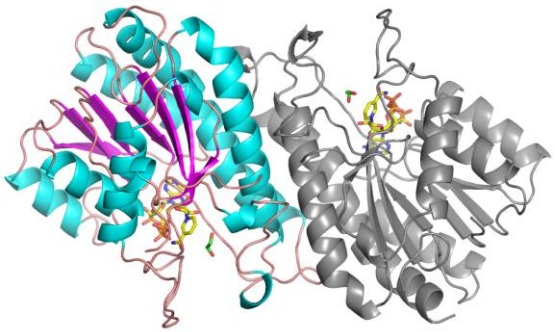

Fig. 1: Overall structure of Tx chicken fatty liver CR. The figure shown is a ribbon representation of the Tx chicken fatty liver CR. The helix and sheet structures are shown in cyan and purple, respectively. The adjacent subunit is shown in gray. NADPH and ethylene glycol are shown as stick model.

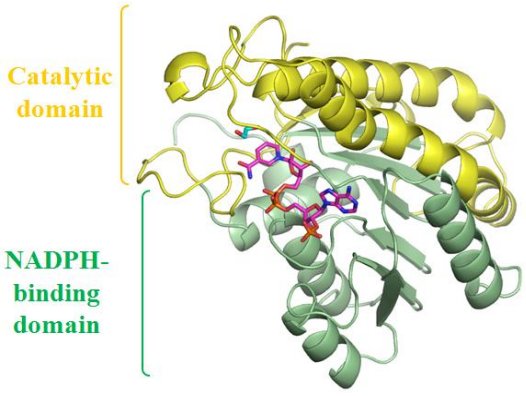

Fig. 2: Monomeric structure of Tx chicken fatty liver CR. The NADPH binding and catalytic domains are shown in green and yellow, respectively. NADPH and ethylene glycol are shown as stick model.

References

[1] K. Yoneda *et al*., *Acta Crystallographica Section F.* (2012) **F68**, 1568-1570.
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* kyoneda@agri.u-tokai.ac.jp