Crystal structure of NAD-dependent glycerol-3-phosphate dehydrogenase from *Leishmania mexicana*

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Introduction

Trypanosomatid parasites are the cause of many severe diseases including African sleeping sickness (*Trypanosoma brucei*), Chagas disease (*Trypanosoma cruzi*), and leishmaniases (caused by members of the genus *Leishmania*). The glycolytic enzymes of the trypanosomes are attractive drug targets since the host-blood-stream form of these parasites lacks a functional tricarboxylic acid cycle and is entirely dependent on glycolysis for ATP production [1]. As part of along term project aimed at developing potent inhibitors against trypanosomal glycolytic enzymes, we have now determined the crystal structure of NAD-dependent glycerol-3-phosphate dehydrogenase from *Leishmania mexicana* (LmGPDH).

Methods and Materials

Crystals of LmGPDH were grown in the presence of $K_2Pt(CN)_6$ and frozen prior to data collection. After an extended x-ray absorption fine structure scan on a frozen crystal to determine the peak and inflection point for platinum, a four-wavelength multiwavelength anomalous diffraction experiment was conducted at the Advanced Photon Source (APS) 19-ID beamline at Argonne National Laboratory. The data were processed with HKL2000 at APS 19-ID. The space group was $P4_12_12$. Cell parameters were a = b = 70.2 Å and c = 210.1 Å. Resolution was 2.2 Å.

Results

A single platinum site was determined from difference Pattersons and its parameters refined before locating two weaker sites from residual Fouriers and including them in the phasing process. The map, calculated to 2.5 Å after solvent flipping with the SOLOMON option in SHARP, was easily interpretable. This map was then used to perform further density modification with the isomorphous native (*apo*) data set using the program WARP. The density at this stage was simply superb. The model was built with O.

Acknowledgments

We thank T. Drmota for his work on the cloning and sequencing of LmGPDH and S. Marché for developing the over-expression system. We thank F. Athappilly for valuable help with computing; C.L.M.J. Verlinde for assistance with modeling; and E.A. Merritt, A. Ævarsson, R. Li, and M. Feese for very useful discussions. Use of the APS was supported by the U.S. Department of Energy, Basic Energy Sciences, Office of Science, under Contract No. W-31-109-Eng-38. We also thank the staff members of the Stanford Synchrotron Radiation Laboratory and the Advanced Light Source for their extensive support with data collection. We would like to acknowledge substantial instrumentation support from the Murdock Charitable Trust to the Biomolecular Structure Center.

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Reference

[1] F.R. Opperdoes, *Annu. Rev. Microbiol.* **41**, 127–151 (1987).