ESRF	**Experiment title:** Serine Hydroxymethyl Transferase (SHMT).	**Experiment number:** LS-855
Beamline: BM14	**Date of experiment:** from: 5 November 1997 to: 6 November 1997	**Date of report:** February 1998
Shifts: *3*	**Local contact(s):** Andy Thompson	*Received at ESRF':* 2 0 FEV. 1998

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Report:

The principal physiological role of serine hydroxymethyl transferase (SHMT; EC.2.1.2.1) is the interconversion of serine and glycine and the generation of one-carbon groups in the form of 5,10-methyltetrahydrofolate. This a crucial intermediate for nucleotide biosynthesis and, as such, SHMT inhibitors have a potential role to play in cancer and antimicrobial chemotherapy. SHMT is a pyridoxal phosphate dependent enzyme which can accept a variety of amino acids as substrates and catalyses aldolytic cleavage, decarboxylation and transamination reactions. The *E. coli* enzyme is encoded by the glyA gene and is a homodimer of subunits, each being approximately 45kDa or 4 17 residues in length.

We have obtained very small crystals of *E. coli* SHMT and have found that these diffract very weakly on a rotating anode source and fade rapidly. However the crystals can be cryoprotected for data collection at 100 K. In this way data to 3.0 Å were collected at ESRF in 1997 from crystals of the apo- and holo- forms of SHMT allowing us to characterise the crystals for the first time. These experiments were performed at beamlines D2AM and BM14 using a CCD and MAR image plate, respectively.

The data we have collected at ESRF establish that the crystals are primitive and belong to the 422 point group with cell dimensions of a=b=104.0 Å, c=150.9 Å. Systematic absences indicate that the space group is $P4_12_12$ or $P4_32_12$. Statistics on these datasets are shown in Table 1.

Table 1. ESRF datasets collected on E. *coli* SHMT.

Crystal	Resolution	R-merge(I)	Completeness	Beamline	Exposures
Apo-SHMT	3.2 Å	14.6 %	99.9 %	D2AM (CCD)	45 s / 0.25 °
Holo-SHMT	3.3 Å	7.2 %	92.0 %	BM14 (MAR)	3 min / °

In the next allocation period we hope to elaborate on the above work by collecting data on heavy atom derivatives of SHMT to facilitate an MIR analysis of its three dimensional structure. The importance of the human enzyme as a potential target for anticancer drugs and the microbial enzyme in biotransformation reactions and as a target for antibiotics means that the structure will have significant biomedical impact.

References

‘Serine hydroxymethyl transferase’. Schirch, L.V. Adv. Enzymol. Relat. Areas Molec. Biol. (Ed. Meister, A.) John Wiley and Sons, New York, Vol. 53, pp. 83-l 12 (1982).