ESRF	**Experiment title: Structural studies Cytochrome c reductase from bovine heart mitochondria**	**Experiment number:** LS-782
Beamline: ID2/BL4	**Date of experiment:** from: 17 Sep.,1997 to: 19 Sep. 1997	**Date of report:** 2/24/98
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Report:

Cytochrome c reductase (also known as Complex III or bc_1 complex) is the middle segment of the mitochondrial respiratory chain which is crucial for aerobic metabolism. Defects in the respiratory chain frequently lead to several mitochondrial myopathies including many neuromuscular disorders such as Parkinson's disease. Bovine heart mitochondrial bc_1 complex, a rather large oligomeric enzyme, is composed of 11 polypeptide subunits having a total combined weight of 240 kDa. The primary sequences of all eleven subunits are known for the bovine heart system. Three of these subunits contain redox prosthetic groups, specifically, cytochrome *b,* cytochrome c_1, and the Rieske iron-sulfur (2Fe-2S) cluster. Cytochrome c reductase is an integral membrane protein complex and is currently the largest membrane protein complex to be crystallized. So far, the high resolution structure of the Rieske iron-sulfur protein (Iwata et *al* , 1996, Structure 4, 567 - 579) and preliminary structure of the complex (Xia, et *al.*, 1997 Science 277, 60-66) have been published. However, the structure of the whole the complex still remains to be completed.

We are currently working on two crystal forms of the *bc*1 complex. One is the hexagonal bipyramid (P6522, a=b=212 Å c=342Å) and the other is the hexagonal rod (P65, a=b= 130 Å, c=720Å). Our strategy is to obtain a MIR phase set from the bipyramid crystals and then extend the phase using multicrystal averaging and, finally, refine the structure using the rod form. In this experiment LS742, we have collected high resolution data sets from both bipyramid and rod forms as well as a series of derivative data sets from bipyramid crystals. The native rod crystals diffracted beyond 2.8 Å, and we have currently processed the data up to 3.0 Å. The native bipyramid crystals diffracted up to 3.0 Å and derivatives have been diffracting up to 4.0 Å. We have summarized the data collection in the table bellow. We were not able to obtain good enough phases for structural determination only from these experiments. This was mainly due to the lack of the isomorphism of the derivative crystals. However, we have obtain a good native set at ID 14 in December 1997 (LS784) which was isomorphic with the derivative sets collected at ID2. Using the data from the both experiments, we could calculate a good MIR phase set up to 4.0 Å which has been extended to 3.0 Å by multicrystal averaging (See the experimental report for LS784). We are currently working on constructing an atomic model for the bc1 complex in the both crystal forms.

Table 1. Summary of the data collection at ID2.

	Res. (Å)	R-merge (%)	Comp. (%)	Riso	Rc (%)	
P6522						
Native* (For phasing)	4.0	5.5(17.4)	84.0(67.1)		-	-
Me3Pb (5mM, 48h soak)	4.0	7.8(19.4)	69.3(34.3)		11.1	0.83
Me3Pb (5mM, 24h soak)	4.0	9.8(25.5)	77.7(52.5)		13.9	0.84
EMTS (0.2mM, 12h soak)	4.0	9.1(21.5)	85.4(66.0)		15.9	0.82
EMTS (0.2mM, 18h soak)	4.0	9.1(23.6)	79.3(55.7)		15.8	0.76
EMTS* (0.2mM, co-cry)	4.0	4.5(25.6)	48.2(37.2)		11.2	0.87
Native (High resolution)	3.0	7.0(26.6)	88.9(76.8)		-	-
P65						
Native (For averaging)	3.0	8.6(23.2)	84.4(42.0)			-

*Data set collected ID14
Numbers in the brackets are for the last shell.