	Experiment title: Structural studies on human monoamine oxidase A	**Experiment number**: MX129
Beamline: ID29	**Date of experiment**: from: 21 June 2003 to 23 June 2003	**Date of report**: 15/7/03
Shifts: 1	**Local contact(s)**: Joanne MCCARTHY	*Received at ESRF:*

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Report:

BACKGROUND - The mitochondrial outer membrane enzymes Monoamine Oxidases A and B (MAO A and MAO B) have been targets for drug research over the past 40 years since they play important roles in the catabolism of neurotransmitters such as serotonin and dopamine. These enzymes are target of antidepressants and neuro-protective drugs against Parkinson's disease and are known to be involved in the clearance of amine-containing xenobiotics. Until this past year, structural determination of either enzyme have been precluded due to their membrane-association and difficulty in purification of sufficient quantities from either animal or human tissues. Recently, we have completed the structure determination of the membrane bound human MAO B (see ESRF HIGHLIGHTS 2002, page 6).

OBJECTIVES - One of the main objectives of the our research is now the elucidation of the three-dimensional structure of human MAO A. The A and B forms of MAO are coded by separate genes and, although they are 70% identical in amino acid sequence, they exhibit different substrate and inhibitor specificities. For instance, serotonin is substrate of MAO A but it is not oxidized by MAO B. These differences are reflected in the pharmacological properties. At present, the principal indication of inhibitors of MAO A is mental depression whereas inhibitors of MAO B are mainly used in the treatment of Parkinson's disease. Understanding substrate and inhibitor specifities among MAOs is the focus of considerable research activity, making the MAO A three-dimensional structure eagarly awaited by researchers.

RESULTS – A key result for the progress of this project has been obtained in that for the first time we have been able to measure a medium resolution data set (3.2 Angstrom) on a human MAO A crystal. This has been made possible by an improved crystallisation protocol combined to the very high brilliance of the ID29 beam line. Based on the measured data, it was possible to solve the structure by molecular replacement.

Although, it will be necessary to improve the resolution, these results represent a milestone for the development of the project in that they show that it is is feasible to grow well ordered diffracting crystals of the protein.