ESRF	**Experiment title:** **Three-Dimensional Structure of Human Monoamine Oxidase A**	**Experiment number**: MX267 MX394

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Report:

Colibus, L., Li, M., Binda, C., Lustig, A., Edmondson, D.E., Mattevi, A. (2005). Three-dimensional structure of human monoamine oxidase A (MAO A): relation to the structures of rat MAO A and human MAO B. *Proc. Natl. Acad. Sci.,* in press

Abstract. The three-dimensional structure of recombinant human monoamine oxidase A (hMAO A) as its clorgyline-inhibited adduct is described. Although the chain-fold of hMAO A is similar to that of rat MAO A and human MAO B (hMAO B), hMAO A is unique in that it crystallizes as monomer and exhibits solution hydrodynamic behavior of a monomeric form

rather than the dimeric form of hMAO B and rat MAO A. hMAO A's active site consists of a single hydrophobic cavity of ~550 $Å^3$ which is smaller than that determined from the structure of deprenyl-inhibited hMAO B (~700 $Å^3$) but larger than that of rat MAO A (~450 $Å^3$). An important component of the active site structure of hMAO A is the loop conformation of residues 210-216 which differs from that of hMAO B and of rat MAO A. The origin of this structural alteration is suggested to result as a consequence from long range interactions in the monomeric form of the enzyme. In addition to serving as a basis for the development of hMAO A specific inhibitors, these data support the proposal that hMAO A involves a change from dimeric to monomeric form through a Glu151Lys mutation that is specific of hMAO A (Hum. Genetics 115, 377-386, 2004). These considerations put into question the use of MAO A from non-human sources in drug development for use in humans.