



	Experiment title: BAG Barcelona – Hydrogen Peroxidase I (HPI)	Experiment number: LS1522
Beamline: ID14-2	Date of experiment: from: 13-Feb-00 to: 15-Feb-00	Date of report: 1-Aug-00
Shifts:	Local contact(s): Laurence Dumon	<i>Received at ESRF:</i>

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Report:

The heme-containing catalase peroxidase HPI is encoded by the *katG* gene from *Mycobacterium tuberculosis* and a related protein is also present in some other bacteria such as *E.coli* and *B.stearothermophilus*. HPI subunits consist of about eight hundreds aminoacids organised in two domains where each domain should bear resemblance to plant peroxidases. Clinical mutations that alter catalase activity in *M. tuberculosis* result in high levels of resistance to INH (isonicotinic acid hydrazide), one of the principal antituberculosis drugs. *HPI* is responsible for the sensibility to INH of *M.tuberculosis* which results from the conversion of the drug into bioactive compounds which interfere with a number of processes involved, in particular, in the mycolic acid synthesis

Crystals from the C terminal domain (the likely INH binding domain) and from the intact homologous HPI protein from *B.stearothermophilus* have been obtained and are now been analysed.

Crystals from the HPI C terminal domain belong to the orthorhombic space group $C222_1$ and have unit cell dimensions of $a=152$. $b=99$. and $c=85$. Å. Crystals diffract beyond 1.4 Å resolution and a complete data set has been collected for the native (though only till 2.3 Å resolution) and for mercury and platinum heavy atom derivatives (only till 3.5 and 4.0 Å resolution, respectively). Crystals containing SeMet have also been prepared though the MAD experiment has yet to be carried out. However, structure determination is now well in progress. Crystals of INH complexes with HPI are also been prepared.