ESRF	**Experiment title:** Dundee-St.Andrews BAG	**Experiment number:** LS-1821
Beamline: ID14-EH2	**Date of experiment:** from: 9 NOV 2000 to: 10 NOV 2000	**Date of report:** 6/3/01
Shifts: 3	**Local contact(s):** Gordon Leonard	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):
Daan van Aalten*, Jukka Taskinen*, Christine Thomas*

Report:

Human Acyl-CoA Binding Protein

Acyl-CoA binding protein is an essential component of the GPI membrane anchor biosynthetic machinery in *T. brucei*. As part of a drug design strategy, we attempted to solve the structure of human ACBP in complex with myristoyl-CoA. The crystals, formed in the presence of zinc ions, were of space group I23 with a=b=c=118.485 Å. Data were collected to 1.38 Å, 100% complete, 4.9-fold redundancy and R_{merge}=5.2%. Investigation of an anomalous Patterson map revealed several strong peaks which were attributed to Zn. Using CNS, this structure was solved by SAD, with 6 zinc sites. The resulting map was of high quality, and warpNtrace was able to build a complete model for both monomers in the asymmetric unit, revealing very strong density for the myristoyl-CoA ligand in the binding pocket. The structure is almost completely refined with SHELX, and a manuscript is in preparation.

Chitinase Inhibitors

Chitinases are key enzymes in the lifecycles of many human pathogens and are therefore an attractive target for selective inhibitor design. Using previous experiments at the ESRF, we collected high resolution data on a chitinase-substrate complex which we have used as a scaffold for design of novel synthetic inhibitors. Using the present shifts, we collected data on 5 chitinase-inhibitor complexes (high resolution limits from 1.45-2.0, R_{merge} from 4.7-11.7 %, all $>$ 95% complete). These complexes are almost fully refined and a manunscript is in preparation.

Photoactive Yellow Protein

PAS domains are sensor proteins involved in sensing of physical signals such as light and oxygen/nitrogen levels. The photoactive yellow protein serves as a structural scaffold for this family of proteins, but has an extra domain which does not occur in other PAS proteins. We have crystallized a truncated version of the yellow protein which we will use as a basis for computer simulation studies into the signalling-related flexibility of the PAS domain. The protein crystallized in $P4_32_12$ with unit cell dimensions a=b=82.57, c=63.45 Å. Diffraction data was collected (in 2 passes) to 1.14 Å resolution (94.4% completeness, R_{merge}=6%). The structure was solved by MR using the native yellow protein structure, and is currently being refined using SHELX.