	Experiment title: ISMB application, Birkbeck; School of Pharmacy & NPP, UCL; Biological and Chemical Sciences, Queen Mary College London. Irving group	**Experiment number**: MX1983
Beamline: ID30B ID23-2 ID29 ID30A-3	**Date of experiment**: from: 21/04/2018 to: 22/04/2018 from: 11/06/2018 to: 12/06/2018 from: 12/07/2018 to: 13/07/2018 from: 1/12/2018 to: 02/12/2018	**Date of report**: 25/02/2019
Shifts: 12	**Local contact(s)**: Leonard G Nanao M De Sanctis D Melnikov I	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

James Irving, University of London UCL, Institute of Structural and Molecular Biology

Report: We have been characterising mutants of the disease-associated plasma protein alpha-1-antitrypsin (AAT) and conformationally-selective antibodies that act as probes of structural change. We have also expended effort attempting to obtain high resolution structures of AAT bound to small molecules, which has necessitated screening of a significant number of crystals. Structures of mutants with substitutions that modify packing in the 'breach' regulatory site of AAT have been solved, as have structures of Fab domains both alone and in complex with AAT. The latter have been used to interpret single-particle reconstructions from negative stain images of oligomers isolated from patients and decorated with Fabs; these data are being written up into two manuscripts which will be submitted in due course. One of the Fab complexes is with an antibody that is being used to screen patient plasma and will represent a third paper.

The following structures have been deposited at the PDB based on ESRF data, with three more to be deposited in due course:

6HX4 "Fab fragment of a native monomer-selective antibody in complex with alpha-1-antitrypsin" ESRF ID30B

6I3Z "Fab fragment of an antibody selective for wild-type alpha-1-antitrypsin in complex with its antigen" ESRF ID29
6QU9 "Fab fragment of an antibody that inhibits polymerisation of alpha-1-antitrypsin" ESRF ID30B