ESRF	**Experiment title: Determination of the structure of cellobiose dehydrogenase from *Phanerochaete chrysosporium*.** BAG: Uppsala (II)	**Experiment number**: LS-1374 a
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Report:

The cytochrome domain of cellobiose dehydrogenase

The fungal oxidoreductase cellobiose dehydrogenase (CDH) degrades both lignin and cellulose, and is the only known extracellular flavocytochrome. This haemoflavoenzyme has a multi-domain organisation with a *b*-type cytochrome domain linked to a large flavodehydrogenase domain. The two domains can be separated proteolytically to yield a functional cytochrome and a flavodehydrogenase. Here, we report the crystal structure of the cytochrome domain of CDH.

The crystal structure of the *b*-type cytochrome domain of cellobiose dehydrogenase from the wood-degrading fungus *Phanerochaete chrysosporium* has been determined at 1.9 Å resolution by means of multiple isomorphous replacement including anomalous scattering information. Three models of the cytochrome have been refined: the *in vitro* prepared cytochrome in its redox-inactive state (pH 7.5) and redox-active state (pH 4.6), as well as the naturally occurring cytochrome fragment.

The 190-residue long cytochrome domain of cellobiose dehydrogenase folds as a β-sandwich with the topology of the antibody Fab VH domain. The haem iron is ligated by Met65 and His163, which confirms previous results from spectroscopic studies. This is only the second example of a *b*-type cytochrome with this ligation, the first being cytochrome *b*562. The haem-propionate groups are surface exposed and, therefore, they may play a role in the association between the cytochrome and flavoprotein domain, and in inter-domain electron transfer. There are no large differences in overall structure of the cytochrome at redox-active pH as compared to the inactive form, which excludes the possibility that pH-dependent redox inactivation is due to partial denaturation. From the electron-density map of the naturally occurring cytochrome, we conclude that it corresponds to the proteolytically prepared cytochrome domain.

Reference: Hallberg, B.M., Bergfors, T., Bäckbro, K., Pettersson, G., Henriksson, G. and Divne, C. (2000). A new scaffold for binding of haem in the cytochrome domain of the extracellular flavocytochrome cellobiose dehydrogenase. *Structure*, **8**, 79-88.