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metals.bbsrcnibb@durham.ac.uk @METALSBBSRCNIBB https://mib-nibb.webspace.durham.ac.uk

New routes for the expression of heme protein targets

"Production of enzymes in quality and quantity sufficient for biophysical and structural analysis has consistently been a major bottleneck for drug discovery efforts. This scheme is hugely welcomed, to help overcome these bottlenecks, not just for my company but for the entire pharmaceutical sector." Andreas Kuglstatter, Roche Innovation Centre

Emma Raven, University of Leicester
Andreas Kuglstatter, Roche Innovation Centre

OUTCOMES: In this project, new expression methods were developed for a range of different heme enzymes that are not readily expressed using conventional methodologies in *E. coli.* Targets from Emma Raven's laboratory were used as a 'test bed' for other heme systems. Human CLOCK protein, which is important in the control of circadian rhythm and thus an important drug target, was included amongst the targets.

INITIAL AIMS: Heme-containing enzymes are a mainstay of industrial biotechnology, and the industry depends on fundamental improvements in methodology emerging from academic groups to harness the potential of their investments in biopharmaceuticals, bioenergy, biocatalysis and drug design. For a number of complex reasons, the interactions between industry/biotechnology and academic laboratories are often less facile and less extensive than they could be, so that new (often specialist and/or unpublished) information is not transferred fluently to industrial partners.

Our overall objective is to use this project to develop new refolding methodologies for expression of difficult (insoluble) heme protein targets, and to set up an on-going dialogue between industrial and academic partners with mutual cognate interests in specific heme enzyme targets. The methodologies that we develop will open up new avenues for industry partners in cases where they have intractable (insoluble) protein targets.

- New expression methods may overcome bottlenecks in drug discovery