Kent and UCB partner on new strategy to boost antibody production

A new partnership between the University of Kent and biopharmaceutical company UCB — funded by a business interaction voucher from Metals in Biology BBSRC NIBB — has identified a potential new way to improve the production of protein-based drugs.

Many drugs that are used to treat cancer and autoimmune disease, as well as insulin, are proteins, and as such need to be made in cells, for example bacteria, mammalian cells or yeast. To function as drugs, proteins must be correctly folded, a process that depends on the formation of disulphide bonds.

Mark Shepherd from the University of Kent, who was the principle investigator on this project, has previously characterised a protein called ScsC (survival of *Salmonella* under copper stress protein, see figure). This enzyme catalyses the formation of disuphide bridges and its activity is influenced by copper.

"The ability of ScsC to facilitate disulphide folding in the *E. coli* periplasm has huge potential for the production of proteins of therapeutic importance."

In this project with UCB, he tested whether the the Scs system and copper could used in *E. coli* to improve the yield of a therapeutically relevant antibody fragment through its effects on disulphide bridge formation.

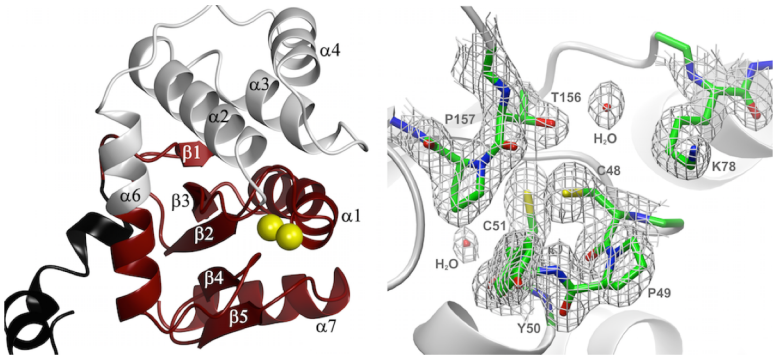
"Improving the yield of correctly-folded antibody fragments (and other high-value proteins) is of clear benefit to UCB," says David Humphreys, industrial partner on this project.

The study used Fab (fragment antigen-binding region) fragments of the breast cancer drug trastuzumab (Herceptin). Compared to full length antibodies, Fab fragments have advantages that include improved specificity, increased delivery options and more economical production systems.

Results from the study showed that Fab fragments of trastuzumab were successfully expressed in *E. coli* periplasm.

"This project has sparked a new relationship with UCB to investigate the potential of our disulphide-folding machinery to assemble a range of protein targets of biotechnological importance," says Mark. Indeed, the partners hope to continue their work to investigate the interaction of ScsC with other protein targets.

"The ability of ScsC to facilitate disulphide folding in the *E. coli* periplasm has huge potential for the production of proteins of therapeutic importance," concludes Mark.



Structure of ScsC, a thioredoxin-like protein of *Salmonella* with a potential role in disulphide folding of therapeutic proteins. Overall protein fold and active site S atoms (yellow spheres) are shown on the left, and the local environment of the CPYC active site is depicted on the right.

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