An express route to biopharmaceutical production

Colin Robinson and Kirsty Richards from the University of Kent have used Business Interaction Voucher funding from BioProNET to work with UCB to test a biopharmaceutical production system in an industrial setting.

The challenge – 'TatExpress' E. coli cells that overexpress the Tat secretion system have an enhanced ability to export recombinant proteins to the periplasm, making this an attractive system for the industrial production of biopharmaceuticals. However, the TatExpress system had not been tested in the fed-batch fermentation systems that are used by industry.

The project – Kirsty worked at UCB to test the abilities of a TatExpress E. coli strain grown in a fed-batch fermentation system to export human growth hormone (hGH) linked to a Tat signal peptide.

Key findings – The work was a complete success; we showed that the TatExpress strains exported at least as much hGH, on a per-cell basis, as they do under the conditions that we had tested previously tested at Kent (i.e., in shake flasks). Exported hGH was by far the most abundant protein in the periplasm. Moreover, the TatExpress cells exported far more protein that the wild type strains, and export levels were equal to those obtained in industrial applications using the alternative Sec-dependent protein export pathway.

The collaboration – Whilst Kirsty was at UCB, she gained hands-on training on the implementation of a scaled manufacturing process of a biotherapeutic. During the collaboration, UCB and University of Kent colleagues shared knowledge, and the project prompted shared participation in the design of further studies.

Outcomes and next steps
• After final experiments, we will submit this work for publication
• Data has been used in an EU grant application involving both partners
• The collaborators are discussing other avenues for follow-on funding

“This is the first demonstration of very high-level export of a biotherapeutic by the Tat pathway in an industrial setting”