Packaging proteins from bacteria: Generation of recombinant outer membrane vesicles for secretion of biopharmaceuticals

The Challenge

The isolation of recombinant biopharmaceuticals from large scale fermentation cultures is a major challenge to industry. The ability to target secretion of recombinant proteins into media is attractive as it improves efficiency and reduces costs. Currently there are no methods for transporting recombinant proteins across the inner and outer bacterial membrane, or for generating vesicles to facilitate the subsequent isolation and purification of the biopharmaceutical from the culture media.

The Research

Dr Dan Mulvihill is a Reader in Cell and Molecular Biology at the University of Kent. In the course of research into the dynamic re-organisation of cellular components within living cells, his group identified a protein that when expressed in the Gram-negative bacteria, E. coli, drives the formation of extracellular vesicles, or exosomes. This provided an exciting potential opportunity for delivering recombinant proteins from the bacteria, into the culture media, to allow simple protein purification, without needing to harvest the cell culture.

The Result

Working in collaboration with Chris Lennon, at Fujifilm-Diosynth, Dan's group generated a series of constructs to test whether this technology could be used to target proteins of interest into the vesicles in both small-scale laboratory and large scale industrial fermentation cultures of E. coli. Using both biochemical and structured illumination microscopy super-resolution imaging techniques, they showed that they were able to deliver the target protein into the cellular vesicles (Figure 1), which could be harvested from the media of active batch scale fermentation cultures.

The Future

With the help of CBMNet BiV funding, Dr Mulvihill has generated exciting proof of concept data, that show it is possible to generate synthetic vesicles into which proteins of interest can be specifically be targeted, to facilitate their subsequent purification. The study generated exciting data that has the potential to be further developed to generate membrane vesicles for drug delivery, vaccination and biopharmaceutical applications.

"The CBMNet network and subsequent BiV funding has enabled me to increase the impact and potential of a discovery made in the course of a BBSRC funded research project. They have led to the development of an exciting new industrial collaboration and have allowed us to acquire proof of concept data validating our system for producing recombinant vesicles for diverse biotechnology applications, and provided the basis for further major research funding applications and future outputs."

Dr Dan Mulvihill, University of Kent