APPLICATIONS FUNDED THROUGH BRIC2 ENABLING GRANT CALL SEPTEMBER 2010

Cold chain storage and distribution of therapeutic mammalian cell cultures, including stem cells, using sol-gel technology			
Dr Che Connon	University of Reading	£80324	BB/I00985X/1
Transport of cell cultures represents a significant distribution problem both for laboratory supply companies and for emerging therapeutics companies in the area of cell therapies and regenerative medicine. None of the current distribution solutions is ideal, involving a combination of complex, specialised, logistics with high costs and/or limited delivery time windows. This project will be aimed at further development of our recently invented novel technology for maintaining mammalian cell cultures in a quiescent state through short term storage and transport. It will be focused on the evaluation of the applicability of this novel technology as an effective ambient and/or cold chain temperature solution to an existing distribution problem affecting a broad range of human/mammalian cell cultures used or intended for use in cell based therapies.			

Microfabricated cantilever methods as nanoscale screens for early indicators of protein aggregation; a feasibility study			
Dr Stephanie Allen	University of Nottingham	£100335	BB/I010645/1
It currently takes over $800 million and around 10-15 years for a new medicinal product to reach the market. Over one third of the products currently under development are biopharmaceuticals; medicines in which the active ingredients are large biological molecules, such as proteins or nucleic acids. Preparations containing monoclonal antibodies (e.g. for the treatment of immune disorders, cancer and infection) are currently the largest, and most important class of biopharmaceutical. The development of biopharmaceuticals is therefore both costly and time intensive. The approaches employed to design/discover new biopharmaceutical agents are very different to traditional synthetic drug-molecule based medicines, with large biological molecules bringing new challenges in terms of development processes during medicine design (formulation), manufacture and storage. At present this is often reflected in the high market price of biopharmaceutical therapeutics, and the pressure to provide cheaper products more quickly has resulted in a demand for new analytical methods/approaches to address issues which conventional drug approaches are struggling to meet. One such issue which directly impacts on protein-based medicines, and which can adversely affect any stage of the development process, is the unpredictable tendency of protein molecules to stick together, to form assemblies of molecules termed aggregates. During medicine manufacture, aggregation can result in highly viscous solutions, causing problems during processing and product packaging. It can also lead to decreased product stability, and hence difficulties in estimating product shelf-life. Within the final medicine, aggregation of the key therapeutic active ingredient can ultimately reduce the efficacy of the medicine and can in extreme cases produce severe unwanted side effects in the patient. By identifying as early as possible within the drug development process, which biomolecules have a tendency to aggregate (and also the conditions which encourage/discourage this aggregation) then the effort, costs and risks to patients associated with development of the therapeutic could therefore be significantly reduced. In this project we aim to explore the feasibility of addressing this difficult challenge, using microcantilever detection approaches (which employ ultrasensitive springs to measure interactions between biological molecules). Ultimately we aim to develop a novel approach to screen potential biological 'active' molecules for their tendency to aggregate through the use of devices capable of detecting the very early stages of aggregation or changes in molecular properties consistent with aggregation behaviour. Within this one year project, our aim is to test and explore the feasibility of a range of potential approaches to achieve this goal. Importantly, our experimental programme will use both model and therapeutically relevant proteins (including monoclonal antibodies). In close collaboration with the pharmaceutical industry			

the devices identified in these preliminary studies will also be assessed for viability and scale up for use in an industrial context. A sizable and increasing academic and industrial community have identified the occurrence of protein aggregation as a critical issue in a number of fields, and have sought new methods to study this phenomenon. This project has the potential to provide an entirely new approach to detecting and investigating the origins of aggregation at its earliest stage. In the longer-term, the work, if built upon will impact upon significant areas of biotechnology and healthcare. Indeed, the methods developed could play an important role in bringing new generation medicines to the market in a cost-efficient and timely manner, and would thus have a very significant impact on public health and quality of life.

Systems optimisation of host cell tRNA usage and codon decoding for the improvement of bioprocessing parameters			
Dr Tobias von der Haar	University of Kent	£66438	BB/I010351/1

The decoding of genes during protein synthesis is a complex process that must occur with great accuracy in order for cells and organisms to remain healthy. Accurate protein synthesis is achieved through the interplay of many different molecules, including ribosomes (the molecular machines that actually achieve protein synthesis), tRNAs (adapter molecules that transport amino acids to the ribosome), and translation factors (helper proteins that establish the correct contact between ribosomes and tRNAs). In order to achieve accurate protein synthesis it is critical that the levels of each of these elements are matched exactly to the frequency with which they are used: if cells contain too much or too little of any of these elements, protein synthesis errors occur more frequently and cellular health declines. In normal cells that only produce proteins from their own genes, the protein synthesis system and levels of the molecules described above are optimised to achieve the required low error rates and high translational speed. However, in industrial applications additional genes are often introduced into cells with the aim of producing specific proteins that are not naturally produced by them. This strategy is used in the pharmaceutical industry to produce the latest generation drugs against cancer, multiple sclerosis and arthritis. When cells make proteins from foreign or artificial genes, the protein synthesis machinery must deal with a situation for which it has not been optimised. We predict that this will increase error rates during the production of the relevant proteins. Protein synthesis errors have negative effects for the ease with which protein-based drugs can be purified and formulated following synthesis in the host cells, and may also adversely affect the potency of the final product. A second prediction we make is that, if we understood the principles of optimisation in detail, we might develop strategies that restore optimal protein synthesis and reduce error rates. Both predictions follow logically from existing knowledge of the translational machinery, although to date they have not yet been experimentally tested and therefore we cannot be completely sure whether they are true. Because our predictions on the relationship between optimised protein synthesis and expression of foreign proteins have important consequences for our ability to make high-quality protein-based drugs, we wish to test them in a small pilot study. We will develop computational models of protein synthesis that will help us to understand the principles of optimisation in protein synthesis. We will then use these models to suggest strategies for achieving optimisation under conditions of foreign protein synthesis in a simple yeast-based expression system. Lastly, we will test experimentally whether these strategies do indeed improve the quality of proteins, and facilitate their processing following synthesis. If this pilot study confirms our predictions, we will use this as basis for a larger study in which we develop optimisation strategies for the various protein synthesis systems used in the pharmaceutical industry.

Real time flux modelling in biopharmaceutical bioprocessing			
Professor Brian McNeil	University of Strathclyde	£98061	BB/I010386/1

Biopharmaceuticals, such as herceptin (trastumazab) which is used in breast cancer treatment, have revolutionised the treatment of many serious diseases, such as solid tumours, leukaemias, degenerative illnesses such as Alzheimer's, and other diseases having complex contributors, such as asthma. However, in addition to being the most potent drugs humanity has ever deployed, these are also the most complex. This implies lengthy development cycles, and very high costs for therapy. A course of herceptin treatment costs around £27,000 per patient. This has led to serious concerns over access to, and availability of these potent drugs. In order to make these complex agents, specially developed (genetically altered) microbial or animal cell systems (expression systems) are cultured in fermenters or bioreactors. But our understanding of how the interaction of the genetic alterations we introduce, and the fermenter or bioreactor environment we culture the cells within, impact upon the cell metabolism is quite limited, especially in early development phase. This lack of clear knowledge about cell metabolism is one major cause of the long, costly drug development cycle of these agents. Our approach is to focus cutting edge techniques upon achieving better understanding of the behaviour of these expression systems early in the development phase. We plan to use non-invasive monitoring techniques (near and mid infrared spectroscopies) actually in the culture vessels together with a previously non real time metabolic analysis tool (flux balancing) to gain real time understanding of the metabolism of these specialised cells when in culture. This technology would give increased knowledge of cell metabolism early in the process cycle, helping accelerate product development, leading to reduced cost therapeutics reaching patients more speedily. This would contribute to increased health in society in general. It would also provide a competitive advantage to the UK biomanufacturing sector involved in making these drugs. In the very near future, this approach could greatly help the development and deployment of specialised cell based therapies (e.g. stem cells). This is especially important as these agents are even more complex than biopharmaceuticals, and have tremendous potential to contribute to enhancing the health and welfare of society in the immediate future.

De novo sequencing of the Chinese Hamster Ovary (CHO) cell genome			
Professor David James	University of Sheffield	£76414	BB/I010610/1

The engineering paradigm of measure, model, manipulate and manufacture underpins the design of products, processes and structures with reliable, predictable performance. The design process requires a detailed knowledge of what the interacting components are, how they interact and the forces (rules) that govern those interactions. This is why it was possible to send a man to the moon in 1969 (i.e. to predict functional performance based on known physical interactions) but not to cure cancer (unpredictability deriving from complex, unknown components and interactions). Accordingly, as we enter a new age of biological engineering, the extent to which it will be possible to engineer complex biological systems for human benefit will ultimately depend upon the extent of our knowledge of those systems - the rules that govern how the complex biological system functions - or malfunctions in the case of disease. To engineer any biological system effectively we need a basic blueprint - knowledge (or design principles) that helps us to understand specifically how that organism is functionally equipped. For biological engineers this primary information is an organism's complete DNA sequence (it's genome). For simple organisms such as bacteria the genome is relatively simple - only about 6000 genes (functional genetic units) in Escherichia coli for example. In human cells there are over 30,000 genes and a large amount of "non-coding" DNA involved in regulation of these genes. Using microbial genome sequence information, bioengineers can for the first time truly engage in the engineering design process. New ways of measuring and modelling the complexity of simple bacterial systems have emerged (this is "systems biology") which enables us to (genetically) manipulate cells and manufacture novel products and processes using new tools (this is "synthetic biology"). Importantly, bioengineers can now predict the functional capability of simple bacteria growing in vitro using computer models. Similar approaches are now being developed for inherently more complex mammalian cells. This project is designed to provide a much needed genomic resource for academic and industrial bioscientists and bioengineers in the UK concerned with the production of a new generation of recombinant DNA derived medicines made by made by genetically engineered cells in culture - biopharmaceuticals. Biopharmaceuticals are proving to be revolutionary treatments for many serious diseases such as rheumatoid arthritis and a range of cancers. We want to determine the genome sequence of an extremely important type of "cell factory" that is used to make these bio-medicines; the Chinese hamster ovary (CHO) cell. Most (60-70%) biophamaceuticals are currently made by genetically engineered CHO cells in culture as well as the vast majority of those in development. However, despite the huge industrial and scientific importance of this cell type, we still do not have the CHO cell's genome sequence: The fundamental informatic resource necessary to utilise new systems and synthetic biology tools to understand and engineer the function of this cell factory. To address this problem we have formed a consortium of the UK's leading academic groups involved in research into CHO cell based manufacturing systems based at the Universities of Kent, Manchester and Sheffield, and four key industrial partners involved in biopharmaceutical manufacturing in the UK. In this project we will utilise the most advanced DNA sequencing technology available to rapidly sequence, assemble and annotate the CHO cell genome. We will establish a network to disseminate this information and to determine how we might most effectively harness this resource for future engineering strategies to improve CHO-cell based production processes. This project is necessary for, and will lead to, cutting-edge applied research underpinning new biopharmaceutical manufacturing technology.

Total £421,575

APPLICATIONS FUNDED THROUGH THE FIRST CALL OF BRIC2
FEBRUARY 2011

Bioprocessing Research For Cellular Products			
Professor Nigel Slater	University of Cambridge	£334600	BB/I016961/1
Dr Karen Coopman	University of Loughborough	£325501	BB/I017062/1

This project aims to develop novel preservation platform technologies required for the successful banking of human cells, an absolute prerequisite for their use as products. Many regenerative medicine products rely on the delivery of live cells to patients. At present this is exemplified by established therapeutic interventions such as bone marrow transplantation, blood transfusion and corneal grafting; future generations of products may include bio-artificial matrices that incorporate donor stem cells, for example bone replacement and repair devices, and artificial 'mini-organs' such as pancreas or liver. Current cryopreservation of stem cell based products results from historic work, using DMSO as a cryopreserving agent which is largely unsubstantiated with respect to final biological activity. DMSO can be toxic to cells, lead to low viabilities post thaw and both genetic and epigenetic instability (i.e. loss of pluripotency) over long term culture. Cryopreservation of blood cells has been attempted previously, with limited success due to loss of cell integrity, primarily due to the breakdown of the cell membrane and consequent loss of overall cell structure. A variety of techniques have been investigated for delivering trehalose, a membrane impermeable cryoprotectant, into mammalian cells, including microinjection, ion channel stimulation, pore formation using mutant bacterial toxins, fluid phase endocytosis, and internal trehalose synthesis via genetic engineering but intracellular trehalose concentrations achieved in erythrocytes has not exceeded 50 mM and is therefore below thresholds for cryoprotection

Biopolymer mediated cell loading achieves substantially increased intracellular trehalose concentrations of up to 251 mM and a concomitant improvement of erythrocyte cryosurvival of up to 20.4 % as compared with conventional methods of loading trehalose into cells. The technology utilizes novel amphiphilic biopolymers that interact with the external cell membrane to enable penetration and retention of cryoprotectant agents into the cells. Membrane permeabilisation by these Cell Permeating Polymers (CPPs) is rapid and completely reversible via washing with buffer. Cellular uptake of trehalose is dependent on polymer molecular structure, concentration, pH, external trehalose concentration, incubation temperature and time. Optimization of these parameters imparts cellular osmoprotection. Overall, a total cell recovery through a single freeze-thaw cycle at -80oC of 82.6 % has been achieved, which compares with a recovery of only 0.8 % for cells frozen in PBS.

This proposal aims to explore the CPP mediated loading of preservation agents into stem cells, to examine preservation by freezing and desiccation and to arrive at integrated processing routes for the preparation of optimally stable stem cells

Developing generic scalable and standardised selection methods for human therapeutic cells			
Dr Eirini Theodosiou	University of Loughborough	£452430	BB/I017143/1
Dr Mark Cobbold	University of Birmingham	£187959	BB/I017151/1

This proposal aims to deliver practical, scientific and technologically innovative solutions to a real problem through partnership between neighbouring Universities: the University of Birmingham, Loughborough University and the University of Oxford. We aim to develop a device to allow blood cells to be selected directly from the blood. This device would allow new treatments to meet the bioselection challenges presented by advanced cellular therapies.

Effective cellular therapies are not new and date back to 1665 when the first successful blood

transfusion took place. Today, 81 million units of blood are taken each year, saving hundreds of thousands of lives worldwide. In addition, at least 50,000 patients receive stem cell transplants (SCT; also known as Bone Marrow Transplants) globally every year (one of the few therapies able to cure individuals with cancer) with each costing around £100,000.

The blood stem cells account for only 0.2% of all white blood cells in the blood. Unfortunately it is not possible to isolate just the stem cells from blood, but instead, a large number of white cells are removed from the donor's blood via a process termed leukapheresis. The donor quickly replenishes their white cells over the next few weeks. One side effect for the donor is that their bone marrow is stimulated to grow which frequently leads to bone pain.

These stem cells potentially offer the gift of life to the recipient who typically will have leukaemia or lymphoma where these cells migrate to the bone marrow and start producing blood for the patient.

However some of the white blood cells from the donor have to potential to cause harm, these immune cells recognise the recipient as foreign and try to attack them. To prevent this, the stem cells are purified from the white cells and infused in a purer form.

Scientists are understanding more about stem cells than ever before and can now expand these rare cells in the laboratory and even create new organs from them (in mice at least). The challenge now is to bring these new techniques and knowledge to the forefront of clinical medicine. Before this can be done, new technologies are required to manipulate these cells in a manner that will not introduce infection and ensures the cells are of sufficiently high quality to be effective for the patient.

The aim of this proposal is to develop a new device which would allow the enrichment of cells. The device will be engineered to be very versatile and would allow the enrichment of any cell type and thus will be of broad interest to many companies seeking to develop cellular therapies. We propose two steps, first a 'capture' device which could even be used to directly isolate cells from the circulating blood of a donor/patient. This could reduce side effects of stem cell isolation such as the bone pain by only picking out the cells of interest. The next step would be to wash these captured cells and pass them over smaller purification columns, which would remove unwanted cell types and capture the cells of interest. This is important as currently there are no ways to select subpopulations of cells. Finally the cells will be released and analysed for their properties. This work has been principally developed by a clinician familiar with the problems delivering new therapeutics to the clinical coalface. We have a working prototype able to capture and release cells from whole blood and are asking for funding to develop this further. We have designed the device with the NHS in mind, to be safe, effective and importantly affordable.

A platform for the optimisation of metabolic pathways for glycosylation to achieve a narrow and targeted glycoform distribution			
Dr Karen Polizzi	Imperial College London	£728580	BB/I017011/1

Recently, the development of treatments for new disease has shifted away from traditional chemical compounds and towards protein therapeutics (biopharmaceuticals) like antibodies for the treatment of cancer and hormones for chronic diseases. Nearly 70% of these protein therapeutics have sugar molecules attached to them naturally which affect their function and how long they remain in the body. Because the sugars are so important for the drug function, one of the biggest problems in their manufacture is how to control what sugars are added (glycoform) and to ensure that all the proteins produced have the same sugars on them (homogeneous glycoform profile). Current production methods yield a non-homogeneous mix of glycoforms. Also, different glycoforms interact with the immune system in different ways, so it would be of benefit to be able to produce certain glycoforms over others depending on what the drug is and how it is meant to function.

Our goal is to develop technology to rapidly determine the effects of different production methods

on which glycoforms are produced and how homogeneous the glycoform profile is. To do this we will develop proteins which are produced inside the cells that are also producing the biopharmaceutical that report the concentrations of nutrients that are already known to influence glycoforms. Alongside, we will develop a computer model of the metabolism of the cells which can predict which glycoforms are produced. Using these two together, we should be able to design new media for the cells to use that result in a more homogeneous glycoform profile which we can change based on what the cells are fed with. We can also suggest genetic changes to the cells that would further help us produce a single, designed glycoform. This could lead to the production of drugs that are safer and require lower doses because they have a single glycoform attached which is the most appropriate for the function of that drug.

Elucidating aggregation mechanisms in antibody fragment-based therapeutics to improve their manufacturability			
Dr Paul Dalby	University College London	£451132	BB/I017119/1

Recent therapies for age-related diseases such as rheumatoid arthritis, macular degeneration, Crohn's disease, and some cancers are engineered forms of biological protein molecules called antibodies that form part of our own natural immune system. Such therapeutic proteins are being derived increasingly from simpler fragments of these antibodies with the hope that this will improve their behaviour in the body, reduce the frequency of injections required, allow them to target new regions of the body, and also allow them to be combined with other biological molecules without becoming too large or unstable. However the manufacturing of therapeutic proteins is extremely challenging due to their delicate and complex nature. Manufacturing processes aim to separate the protein molecules from the rest of the cellular components in which they were synthesised, to obtain extremely pure therapeutic material that is suitable for use in humans as a therapy. However, the processes available for large-scale manufacture place a great deal of stress on the protein due to changes in temperature or acidity, the addition of salts, the use of mechanical agitation, rapid changes in the rate of flow through machinery, and the interaction of proteins with air bubbles. This frequently causes the protein to deform slightly and to subsequently stick together to form tiny particles called aggregates. While these are often not visible to the naked eye, their presence in therapies can be hazardous to patients as they may cause severe inflammation and potentially more deadly immune responses. Therefore, one of the key challenges that the bioprocess development and therapeutic protein manufacturing industries would like to address is to be able to either predict the conditions that cause a protein to aggregate, or to increase their robustness so that they aggregate less frequently during their manufacture.

We aim to carry out and demonstrate a suite of rapid experimental measurement techniques that allow a new therapeutic protein to be evaluated quickly for the conditions in which they have a greater tendency to form aggregates. The conditions to be tested will be same as those used throughout bioprocess manufacturing, and will therefore allow bioprocess engineers to rapidly identify the conditions in which their manufacturing processes will be best operated, or whether the protein is unlikely to be manufacturable. Having quickly determined the conditions at which the protein begins to form small and soluble aggregates, we will also carry out a detailed molecular analysis of the structure of proteins at these conditions and also those either side in which the protein remains in solution as a single molecule, and where it forms larger aggregates. This will allow us to see what changes in the protein structure occur before, during, and after the aggregation is initiated and therefore deduce which events are on the critical path to aggregate formation. Having achieved this we will then be able to target changes to the protein called mutations that will interfere with and suppress the aggregation process. Finally, by comparing a related set of therapeutic antibody fragment proteins, we will gain insight into those factors that are specific to each protein type, and those that occur more generally and hence become useful targets for the future engineering of therapeutic protein designs. It will also allow others to improve their mathematical modelling methods that aim to predict whether proteins will aggregate

under certain conditions.

Predictable Protein Production			
Professor Hans Westerhoff	The University of Manchester	£653032	BB/I017186/1

Specific proteins including biopharmaceuticals (=protein-based medicines), protein-based specific probes, and enzymes, constitute a growth market. Their complexity allows these agents and reagents to be highly specific, and thereby, for instance, kill diseased cells whilst leaving healthy cells intact. In addition, the fact that they are composed of the 20 natural amino acids offers an important aspect of safety; they essentially consist of natural compounds that can be degraded safely. The complexity of these products is well served by the complex production environment of living cells. This comes at a price however: Living cells are difficult to manage with simple methodologies, and difficult to understand with the traditional molecule or whole cell focused biologies. Protein production by living cells is unpredictable and rather inefficient, making biopharmaceuticals more expensive than they should be, to the extent that some cannot be produced economically.

Systems Biology is a recently amplified scientific discipline studying how the complex intracellular networking of molecules controls the functioning of whole living cells. The UK is among the word leaders in this Systems Biology, with its 6 government (BBSRC+EPSRC) funded Centres for Integrative Systems Biology and three such Doctoral Training Centres. One of these research centres, the MCISB at the University of Manchester, which also hosts one of the DTCs, has put together a complete tool set enabling the understanding of the growth of baker's yeast, which is one of the most famous and useful living cells (bread, beer and wine). Manchester is also home to the Centre of Excellence in BioPharmaceuticals (COEBP), in which the production of biopharmaceuticals by mammalian cells is being studied. This research project does the obvious: it brings together the MCISB and the COEBP. It does this in the context of the Biotechnology Research Industry Club (BRIC) in which academics and industrialists meet to discuss how science and engineering can be implemented to lead to work that is better for the public, through better industrial processes. The idea is to throw the new Systems Biology at the problem of understanding the living cells whilst producing proteins. This will first be done for the better known yeast cells, now producing proteins rather than beer, but immediately thereafter the same approaches will be implemented in mammalian cell lines that are known to produce less protein but in better shape. If successful, this will give Britain a world leading role in the production of biopharmaceuticals through the mathematical modelling of the production processes that occur in the cell factories. Enabling maximal efficiency and control, the bioprocess industry associating with BRIC will become highly versatile and quick in designing and optimizing processes for a great variety of biopharmaceuticals. This could not now be accomplished in other countries. This increased versatility may lead to a substantial augmentation of bioprocessing in the UK process industry.

The project is extremely challenging and interesting scientifically. One thing is that for the mammalian cells, the available information is limited: The structure of their DNA is not precisely known. Modelling methods will therefore have to be used that reckon with the many possible DNA structures. This requires substantial computer power and adeptness of the programmer. Another challenge is to measure precisely the chemical activity of the protein producing cells and use the results to deduce which parts of their networks they are using to produce the protein. This should enable us to predict their maximum efficiency and then perhaps to direct them to improved performance. Because Life is subtle, yet another challenge is to cultivate the cells in such a way that they 'feel cool' when they are producing 'hot' protein for us, thereby preventing them from resisting doing their job well.

Understanding and predicting aggregation in biopharmaceuticals			
Dr Robin Curtis	The University of Manchester	£577798	BB/I017194/1
Currently, one of the bottle necks to developing cheaper protein therapeutics is the cost of the downstream bioprocessing and formulation steps. A key problem is the loss of active protein therapeutic to irreversible aggregation throughout the bioprocess. Other problems can arise during chromatography or filtration when encountering high protein concentrations which could lead to high viscosites or even precipitation. The focus of this work is to develop predictive methods for identifying problematic conditions early on in the bioprocess. These could then be used for identifying changes to the protein to minimize the problems. Alternatively, the method could be used for optimizing the solvent properties (pH, buffer type and concentration) or finding other small molecule additives to be used in order to avoid aggregation or increase protein solubility. We benchmark our approach by studying antibodies and antibody fragments due to their growing importance as human therapeutics.			

Total £3,711,035

APPLICATIONS FUNDED THROUGH BRIC DOCTORAL PROGRAMME FEBRUARY 2011

Academic Institution	Project Supervisor	Project Title	Sponsoring Company
UCL	Dr Suzanne Farid	Linking High Throughput Cell Culture, Multivariate Analysis and Economics for More Effective Process Integration	Medimmune
UCL	Dr Paul Dalby	Microscale freeze-dried and liquid formulations of therapeutics to investigate the relationship between forced degradation and long-term shelf life	NIBSC/HPA
UCL	Dr Daniel Bracewell	Understanding on-column protein aggregation and its impact on bioprocessing	UCB Celltech
Manchester	Dr James Warwicker	Controlling liquid-liquid phase separation in antibody formulations	Medimmune
Manchester	Professor Hans Westerhoff	Protein burden in protein overproduction	Fujifilm Diosynth Biotechnologies
Imperial	Dr Cleo Kontroavdi	Development of a computational tool for predicting the impact of bioprocess conditions on protein glycosylation	Medimmune
Nottingham	Dr Stephanie Allen	Development of single molecule assays for the detection of aggregation within high concentration protein therapeutics	Pfizer
UCL	Dr Eli Keshavarz-Moore	An upstream platform for the production of high grade heterologous proteins in Pichia pastoris	Fujifilm Diosynth Biotechnologies