

Discovering more with less

Global biopharma company UCB has increased the throughput of its antibody purification pipeline, using a flexible Freedom EVO® workstation to miniaturize its chromatography applications. As a result, the Company is able to investigate far more parameters in a fraction of the time, while consuming significantly less material.



UCB is a global biopharmaceutical company, with operations in approximately 40 countries. It focuses on antibody-based drugs for the treatment of autoimmune diseases, such as Crohn's and rheumatoid arthritis, and conditions affecting the central nervous system. UCB's immunology hub is based in Slough, UK, where the majority of the Company's antibody research and early development takes place.

Research teams at UCB identify novel targets and specific antibodies using two different cell-based approaches for protein production, *E. coli* and Chinese hamster ovary (CHO) cells. Antibodies are then handed over to development teams to progress through the pipeline. Jonathan Symmons, Development Scientist at UCB, explained: "Our role is to develop the best processes for generating large amounts of the antibody drug product in house, and we are closely involved in both Phase I and Phase II clinical trials, where the process is still open to change and further development."

Purification is a significant stage of the manufacturing process, and the UCB team primarily uses chromatography techniques to purify the products from the harvested

cell cultures and microbial extracts. They are constantly looking at ways to scale this process down to reduce the amount of material used, giving them the opportunity to perform more experiments with the amount of protein available. This is partly to do with cost, but also because they are frequently working with very small sample sizes. For example, in early phase projects they might screen a few similar but slightly different constructs of an antibody. At that stage, the fermenters are not optimized to produce huge amounts of material, and only milligrams of antibody are coming through.

"We had been looking at Atoll's MediaScout® RoboColumns® for some time, and specifically at how to implement them into an automated protocol. Atoll and Tecan had worked together closely on this, and it made sense to look at this option; the support we subsequently had from both companies in setting up and optimizing the system was


excellent. We soon realized how flexible the Tecan system is and eventually chose a configuration that would not only allow us to switch between chromatography and ELISAs, but would also still keep our options open for other potential assays. Our Freedom EVO 200 is equipped with a Te-Stack™, a Liquid Handling Arm with eight fixed tips, a Robotic Manipulator Arm, a Te-Shake™, a HydroSpeed™ plate washer and Infinite® 200 PRO microplate reader. We also have a Te-VacS™ vacuum manifold module, and are looking to implement the 96-well PreDictor™ filter plate chromatography format (GE Healthcare) to further reduce the amount of material required and potentially provide a screening technique for even earlier-stage products."

The workflow varies from day to day; the group may be looking at different loading conditions, varying the pHs, conductivities, etc. for a single column type, or screening

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Left to right: Jonathan Symmons, Chris Morris and Mariame Dami



resins with different loading material. More and more people at UCB are being trained to use the Freedom EVO for applications at all stages of the development process, and there have recently been two Masters' students performing a large Design of Experiments (DOE) study to assess the Freedom EVO for the chromatography capture steps in early phase process development. Full analysis of the project is not yet complete, but early indications suggest that this approach is comparable to previous methods.

Thanks to the Freedom EVO platform, the

DOE study was on a far larger scale than had ever been practical for the development team to undertake before. Jonathan continued: "The sheer volume of experiments we can now perform simultaneously is brilliant. We can do eight chromatography runs at once using the RoboColumns, but the DOE project was even more impressive. We have been able to perform full factorial DOE – previously this would have been performed as a fractional factorial providing less than a third of the data points – and we could never have even attempted that without the Freedom EVO and RoboColumns; there simply would not have been enough

material or time in the early phase of a project."

Time is also a critical factor for EngD student Chris Morris, who is using the liquid handling capabilities of the Freedom EVO to look at precipitation as a purification method. This project compares different permutations for precipitating the target protein from the process impurities, and requires mixing hundreds of combinations of buffers. This would take days to perform manually at the bench, but only takes hours in a microplate on the Freedom EVO, again using smaller sample volumes.

Jonathan concluded: "The whole industry is moving towards a 'Quality by Design' approach to development, and the Freedom EVO fits this model perfectly. It enables us to perform large DOE studies with smaller amounts of material, in a shorter amount of time, resulting in a greater understanding earlier in the development phase and potentially minimizing the number of changes to the process later on in the pipeline. We are doing things that we never would have attempted before, which is a huge step in the right direction."

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UCB's Freedom EVO workstation offers flexible automation for assay design and optimization