Identifying universal bottlenecks in CHO cell clones and pools for informed host cell line development

Utilising Silvia Bio's cell profiling platform to identify production bottlenecks in a CHO host cell line

Project background

This case study highlights a collaboration between Silvia Bio and a multinational biopharmaceutical company. The focus of this project was to identify production bottlenecks in various CHO cell lines and a cell pool, each producing different antibody formats that varied in production complexity. The aim was to discover non-product specific bottlenecks, enabling the engineering of the host cell line to better support the production of diverse 'next generation' antibody formats.

Project outline

Silvia Bio performed the cell profiling workflow on four antibody-producing cell lines and a cell pool expressing a particularly challenging antibody. All of these were derived from the company's proprietary host cell line. For this project, 53 'control nodes' were introduced into producing cell lines and pools. These nodes target 12 cellular pathways that are critical for production. By dysregulating the cells with various control nodes, the manufacturing performance of the cells can be analysed.

Project results

The profiling results are anonymised to maintain the confidentiality of the partnering company. Figure 1 (overleaf) shows the results from the profiling panel introduced into all cell lines and the cell pool. Of the 53 control nodes tested, 34 showed a significant change in titre compared to the GFP control in at least one cell line or pool. Moreover, six control nodes emerged as potential cell engineering targets to improve the company's CHO host, as they led to significant changes in titre in at least three cell lines or pools. Control node 1 and 2 were the most promising targets, leading to significant titre changes in all tested cells. In contrast, the remaining 19 control nodes (not shown in Figure 1) did not result in titre changes that deviated significantly from the GFP control in any of the tested cells.

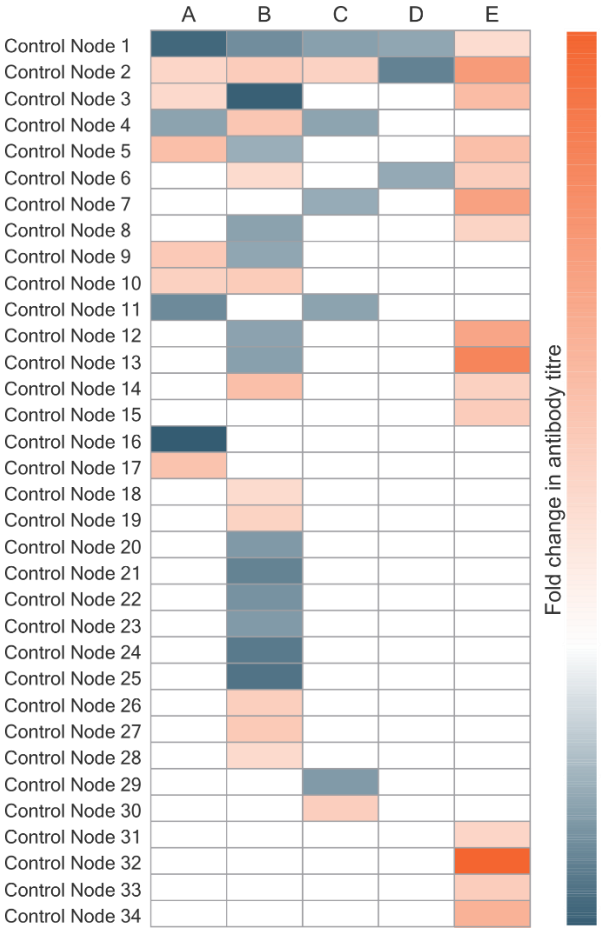

Figure 1. Changes in antibody titre following the cell profiling workflow. Profiling was performed on four antibody-producing cell lines (A–D) and one cell pool (E). Values represent the mean of three independent experiments (n = 3, each performed in triplicate). Data are presented as normalised titres relative to a GFP control and are ordered by the number of cell lines or pools affected. Only control nodes that resulted in a significant change in titre in at least one cell line or pool are shown.

Project conclusion

The profiling platform rapidly identified six control nodes that led to changes in titre in the majority (>3) of tested cell lines and the cell pool. These nodes are likely linked to bottlenecks specific to the company's CHO host cell line, independent of the antibody format expressed, making them promising targets for cell line engineering. Nearly one-third of the tested control nodes did not result in a significant change in titre, indicating that the host cell's capacity to express recombinant products is not limited by these pathways and would not benefit from engineering. Additionally, 28 control nodes led to product-specific changes in titre. While these could be targeted to improve the production of specific antibodies, they are less relevant for universal host cell line improvement.

Future directions

The partnering company is using the responsivity data provided by the cell profiling workflow to guide genetic engineering strategies aimed at improving host cell capacity for antibody production. Furthermore, a follow-up study has been agreed upon to evaluate potential titre improvements by applying chemical modulators that are universally applicable across all cell lines and pools derived from the company's CHO host cell line.