DCU INVENT
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Dublin City University Licensing Opportunity

LIFE SCIENCES

Novel Selection System for host cells

INTRODUCTION

The National Institute for Cellular Biotechnology (NICB) at DCU is a multidisciplinary centre of research in fundamental and applied cellular biotechnology, molecular cell biology, ocular diseases and biological chemistry. It employs a highly skilled team of cell and molecular biologists, biotechnologists, chemists and computer scientists. The **CHO cell engineering group** at NICB is a highly regarded research team focused on investigating the cellular molecular biology of CHO production systems.

BACKGROUND

Animal cells, especially Chinese hamster ovary cell lines are the most important production vehicle for making recombinant human proteins, such as cytokines and antibodies for human therapeutic use. Most selection systems currenly used to enrich for CHO cell lines, transfected with a cDNA encoding a biopharmaceutical or other protein, use a cytotoxic drug as selective agent. This has a number of disadvantages including possibility of random mutagenesis and cannot be used in-process because of toxicity. The **CHO cell engineering group** at NICB have developed a novel nutrient deprivation system based on a putrescine starvation system.

TECHNOLOGY DESCRIPTION

Polyamines have essential roles in cell proliferation, DNA replication, transcription, and translation processes, with intracellular depletion of putrescine, spermidine, and spermine resulting in cellular growth arrest and eventual death. Serum-free media for CHO-K1 cells require putrescine supplementation, because these cells lack the first enzyme of the polyamine production pathway, arginase. On the basis of this phenotype, we developed an arginase-based selection system. We transfected CHO-K1 cells with a bicistronic vector co-expressing GFP and arginase and selected cells in media devoid of l-ornithine and putrescine, resulting in mixed populations stably expressing GFP. Moreover, single clones in these selective media stably expressed GFP for a total of 42 generations. Using this polyamine starvation method, we next generated recombinant CHO-K1 cells co-expressing arginase and human erythropoietin (hEPO), which also displayed stable expression and healthy growth. The hEPO-expressing clones grew in commercial media, such as BalanCD and CHO-S serum-free media (SFM)-II, as well as in a defined serum-free, putrescine-containing medium for at least 9 passages (27 generations), with a minimal decrease in hEPO titer by the end of the culture. We observed a lack of arginase activity also in several CHO cell strains (CHO-DP12, CHO-S, and DUXB11) and other mammalian cell lines, including BHK21, suggesting broader utility of this selection system. In conclusion, we have established an easy-to-apply alternative selection system that effectively generates mammalian cell clones expressing biopharmaceutically relevant or other recombinant proteins without the need for any toxic selective agents. We propose that this system is applicable to mammalian cell lines that lack arginase activity. It's USP is that this technology provides a new selection method for CHO cells transfected with an exogenous gene without the requirement to add toxic chemicals

RESEARCH AND IP STATUS

Priority Patent application filed August 2019 - UK - No. 1911023.8

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TYPE OF BUSINESS SOUGHT

Available for licensing. We are also interested to talk to companies interested in collaborations and strategic partnerships.

CONTACTS

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