DECISION-SUPPORT TOOLS FOR COST-EFFECTIVE BIOPROCESS DESIGN IN THE CELL THERAPY SECTOR

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Key Words: Cell therapy, bioprocess economics, decision-support tool, bioprocess design, commercial production

It is important to make effective decisions as to manufacturing strategies and process designs early on in product development; failure to do this may result in costly and time-consuming bridging studies during clinical trials and inflated manufacturing cost of goods (COG). Decision-support tools can aid the design of cost-effective bioprocesses via the quantitative evaluation of both financial and operational aspects of manufacturing strategies and bioprocess designs.

A range of decision-support tools, developed at University College London, will be presented and applied to industrially-relevant case studies to demonstrate their applicability to cell therapy manufacturing. The first case study focuses on bioprocess design for a SC-based therapy; equipment sizing and selection of optimal technology platforms will be considered. Directed and spontaneous differentiation protocols are compared from an economic perspective and the production scales where microcarrier-based differentiation prove more cost-effective than planar options are highlighted. In the final case study, bioprocessing of an allogeneic CAR T-cell therapy is considered. Different bioprocess flowsheets are evaluated from both an economic and operational perspective in order to identify the optimal bioprocess design based on multiple criteria. The effect of variation in key process parameters upon the manufacturing COG is considered alongside windows of operation whereby a satisfactory COG to selling price ratio can be achieved.

The methods presented link advanced bioprocess economics models with stochastic analyses, brute-force search algorithms, evolutionary optimisation, and multi-attribute decision making. Research outputs include the identification of key process economic drivers and process bottlenecks. Future process improvements required in order to create financially feasible cell therapy bioprocesses are also presented. Stochastic modelling has been used in order to provide risk-adjusted analysis of manufacturing strategies and process designs. Finally, multi-attribute decision making has been employed in order to evaluate process designs from both a financial and operational perspective. This work presents a range of computational techniques which can be applied to bioprocess design problems in order to achieve cost-effective, robust bioprocess designs early on in process development.