

METABOLOMICS AND THE ROLE OF METABOLISM IN STEM CELL BIOPROCESSING

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Stem cell bioprocesses require reproducibility, robustness and quality control of both the process and the product for wide clinical use¹. The role of metabolism is critical in stem cell bioprocesses as it controls cellular processes (proliferation, apoptosis, reprogramming) but also influences gene regulation and cellular physiology by directly affecting epigenomic changes². Metabolomics analysis of both intracellular (finger-printing) and extracellular (foot-printing) metabolites a) enables evaluation of “cellular state”, b) captures a holistic view (snapshot) of the cell culture physiology, and c) provides dynamic information culture needs that can be used for bioprocess optimisation. Examples of research conducted in our group highlight 1) that metabolic profiling was able to identify differences in human pluripotent cell physiology (hESCs and hiPSCs) after treatment with ROCK inhibitor, which control gene expression and protein expression was not sensitive enough to detect; 2) time-series metabolomics analysis of the osteogenic differentiation process of umbilical cord blood mesenchymal stem cells identified differences in the efficiency of two major osteoinductive agents (dexamethasone and BMP-2) demonstrating that dexamethasone-treated MSCs were metabolically close to human primary osteoblasts; 3) the development of a novel perfusion bioreactor for the culture of pluripotent stem cells (ESCs) that facilitates environmental homeostasis by maintaining sufficient levels of nutrients while preventing the accumulation of metabolic by-products over toxic levels ensuring ESC pluripotency. The above examples emphasise the importance of metabolomics in all stages of stem cell bioprocess by sensitive and effective monitoring, which can be used for robust bioprocess optimisation as well as bioprocess and product quality control – critical aspects of biomanufacturing for clinical applications.