Human iPSC-Derived Cells for Modelling Cellular Bioenergetics: Building a Metabolic Profile Using the XF Mito Stress Test

Abstract

Altered cellular bioenergetic events due to metabolic dysfunction have been implicated in numerous pathophysiological conditions. The metabolic profile of a cell can differ from one cell type to another, illustrating the importance of selecting a physiologically relevant cell model. Primary cells can offer relevant human biology, but issues with cell quality, availability and donor-to-donor variability continue to limit their large-scale implementation in vitro. Cellular Dynamics International (CDI) has developed a manufacturing pipeline to reproducibly generate commercial quantities of high-quality, highly pure terminally differentiated human cell types derived from induced pluripotent stem cells (iPSCs). (CellCardiomyocytes, CellNeurons, and CellHepatocytes are among all cell types produced by CDI). In this study, the XF Extracellular Flux Analyzer was used to determine whether the Cell human cells represent a physiologically relevant cell model to study cellular metabolism. (Cell Cardiomyocytes, Cell Neurons, and Cell Hepatocytes were cultured directly on XF Cell Culture Microplates and baseline oxygen consumption rates were measured. Following culture optimization, oxygen consumption levels were obtained that enable the interrogation of metabolic function with the XF Mito Stress Test. ATP, respiration, and OCR were measured to chemical modulation of mitochondrial function as expected. Using the optimized culture and chemical compound conditions, mitochondrial ATP production and maximum respiratory capacity were measured to establish metabolic profiles. The data were consistent across manufacturing batches, demonstrating both assay-to-assay and lot-to-lot reproducibility. Together, Cell human cells and the XF Extracellular Flux Analyzer offer an excellent in vitro platform for analyzing mitochondrial function, understanding pathophysiology, and evaluating therapeutic interventions in biologically relevant human cell types.

Human iPSC-Derived Cells as a Model System

The ability to reprogram adult somatic cells (e.g., skin, blood into iPSCs has created tremendous interest and excitement since described in 2007. For decades, researchers have relied on short-lived primary cultures or animal models to dissect the mechanisms and pathogenesis of disease. Now, differentiated cells derived from iPSCs have the potential to provide a readily available source of well-characterized human cells for preclinical drug screening, safety testing, and disease modelling. CDI has contributed to the field by developing a manufacturing pipeline with improved iPSC technology that enables large-scale production. Saphon Biosciences for the high-purity, physiologically relevant human cells for disease research and drug development.

Preclinical Trials

ICell Human Cells Exhibit Robust Metabolic Profiles

ICell Human Cells Exhibit Lot-to-Lot Reproducibility

ICell Human Cells Exhibit Cell Type-Specific Bioenergetic Profiles

The Power of iPSC Technology

The discovery that human adult cells (e.g., skin, blood) can be induced to become stem cells capable of differentiating into any cell type in the body (e.g., heart cells, neurons, liver cells) has launched a new era of biomedicine with unprecedented opportunities to advance the fields of drug development, disease research, and regenerative medicine. iPSCs offer two key advantages over other in vitro models:

1. iPSCs can be differentiated into any of the 200+ cell types in the human body.
2. iPSCs can be derived from any individual or patient population using non-invasive methods.

To realize the full potential of iPSC technology, CDI has developed a manufacturing infrastructure to enable large-scale, reproducible production of high-quality, physiologically relevant iPSC-derived human cells from panels of donors that represent ethnogeographic diversity and disease phenotypes.

CDI offers custom MyCell™ services to reprogram patient samples to iPSC cells and differentiate them to various cell types. The addition of this service delivers the robust and scalable manufacturing capabilities of CDI to the individual investigator, providing a powerful and consistent source of material to begin asking more advanced questions of human biology.

Summary

The XF Extracellular Flux Analysers combined with CellCardiomyocytes, iCell Neurons, and iCell Hepatocytes, offer a powerful tool to investigate bioenergetics in human cells. Robust procedures for studying the metabolism of iPSC cells with this instrument platform have been generated. The data show that iCell human cells provide a readily available, biologically relevant, and reproducible cell model for studying cellular metabolism. Importantly, this study creates a foundation for more advanced studies of cellular respiration or other metabolic endpoints.

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