In-Line monitoring of culture medium using Live cell metabolic analyzer

Introduction

Within the fields of cancer immunology, including CAR-T therapy, and regenerative medicine using stem cells such as iPS cells, understanding cellular metabolism is becoming an important factor in a wide range of areas, including basic research in pathological analysis and investigation of production processes for pharmaceutical product formulation. Until now, component analysis of culture medium has been carried out by periodic sampling, but in basic research and in the small-scale process development phase, only a small amount of sample can be collected. Furthermore, since sampling only provides measurement data from at most a few time points per day, it does not give an accurate picture of changes in the state of cells during culture.

In the present study, we used a Live cell metabolic analyzer to continuously measure glucose and lactate levels while culturing Jurkat cells, in order to investigate the accuracy and stability of PHC's proprietary In-Line sensor.

The PHC Live cell metabolic analyzer

One of the main pathways in cellular energy metabolism is glycolysis. During the glycolytic process, glucose in culture medium is taken up into cells and lactate is produced. Using a proprietary In-Line sensor adapted from electrochemical sensor technologies cultivated by PHC in the field of blood glucose measurement, researchers at PHC have engineered an analyzer capable of highly accurate and continuous monitoring of glucose and lactate concentrations in culture medium while cultivating cells in a 24-well plate, without the need for sampling. This analyzer makes it possible to measure metabolic changes as continuous linear data rather than at just a few time points per day. Also, because the device analyzes glucose taken up by the glycolytic pathway and lactate produced as a result, changes in glycolysis can be directly evaluated.

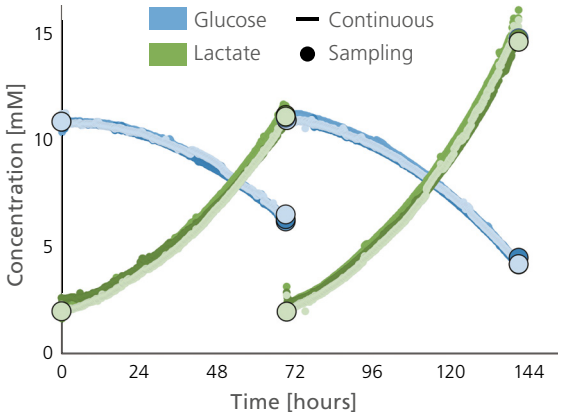
Method

The Live cell metabolic analyzer uses electrochemical sensors to obtain electric current values corresponding to the concentrations of glucose and lactate. Before the samples are measured, a calibration curve for evaluating and converting the relationship between current and concentration is created from measurements using culture medium with known glucose and lactate concentrations.

In this experiment, Jurkat cells (ATCC: TIB-152) were cultured in RPMI 1640 Medium in 24-well plates. Glucose and lactate concentrations were continuously measured for a total of 6 days using the Live cell metabolic analyzer. The Jurkat cells were reseeded on day 3, the medium was sampled at the time of reseeding, and the accuracy of measurements was evaluated by comparing concentrations converted from current values measured by the Live cell metabolic analyzer with concentrations measured by colorimetry.

Result

To evaluate the measurement accuracy of the Live cell metabolic analyzer during cell cultivation, Jurkat cells were cultivated and continuously monitored over a 6-day period using the Live cell metabolic analyzer. During the 6 days of cell proliferation, the concentration of glucose in the culture medium decreased as glucose was consumed, and the concentration of lactate in the culture medium increased as lactate was produced. These increases and decreases in concentrations could be depicted as continuous changes based on the acquired data. The discrepancy with sampling data from colorimetry of media collected 3 and 6 days after cell seeding was 92-110%.



Conclusion

The Live cell metabolic analyzer was able to measure concentrations of glucose and lactate in the range of 4-11 mM and 2-15 mM, respectively, for 6 days continuously, with a maximum discrepancy of 10% when compared to sampling data measured by colorimetry. Moreover, when Jurkat cells were cultivated in RPMI 1640 Medium, changes in glucose and lactate concentrations in response to changes associated with cell proliferation could be depicted as continuous data.

These results indicate that the Live cell metabolic analyzer can be utilized for evaluating changes in cell metabolism over time by continuously measuring glucose and lactate concentrations in culture medium and is therefore capable of monitoring cell metabolism without the need for periodic sampling.

PHC Europe B.V.
Nijverheidsweg 120 | 4879 AZ Etten-Leur | Netherlands
T: +31 (0) 76 543 3839 | F: +31 (0) 76 541 3732
www.phchd.com/eu/biomedical