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John Carvell

Aber Instruments, johnc@aberinstruments.com

Aditya Bhat

Aber Instruments

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MONITORING LIVE STEM CELLS IN SUSPENSION AND ATTACHED TO CARRIERS IN CONVENTIONAL AND SINGLE USE BIOREACTORS

John Carvell, Aditya Bhat,
johnc@aberinstruments.com
Aber Instruments Ltd., UK

Embryonic stem cells are promising cell sources for regenerative medicine and organ replacement after disease or injury. Traditional single use bioreactors such as the Sartorius Biostat Rocking Motion bag are being used for growing up these cells at the larger scale and a number of companies are developing fully automated, closed bioreactor systems specifically for growth of stem cells for clinical applications eg Xpand (Holland), Pall(USA).

The stem cells in the bioreactors need to be monitored and controlled for both product quality and to satisfy GMP requirements and one of the most important parameters is the concentration of live cells. On-line monitoring of the live cell concentration can be used to monitor process irregularities, define when sufficient cells are available for the patient or it might be the trigger point for providing additional feed to the bioreactor. It can also save costs as the information can be used to abort the cell culture or optimize the process.

Sampling for cell concentrations should be avoided to eliminate the risk of contamination. Moreover, with stem cell cultures once embryoid bodies form it is both difficult to take a representative sample and to get a true cell count using a trypsin pre-treatment. The same problems occur if the cells are grown on micro-carriers. Ideally the cell concentration should be measured in real time using a non-invasive sensor and Radio Frequency Impedance (RFI) spectroscopy is a very promising tool for this application. RFI is already widely used in large scale GMP suspension and micro-carrier cell culture and single use probes have been developed by Aber Instruments (Aberystwyth, UK).

In this poster, we provide a number of examples of how RFI has been used to monitor and control stem cell cultures in bioreactors up to 1L in volume. The performance of a disposable biomass probe to measure mesenchymal stem cells grown on micro-carriers in a rocking motion bag will also be presented.