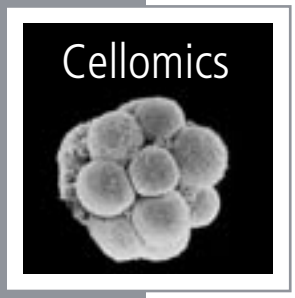

Fully Automated System for Adherent Cell Cultures

The set of all states that a particular cell can enter is known as the cellome. Cellomics, the study of particular cellomes, is one of the emerging fields in bioscience.

The technical application of cellomics research depends on the stable and reproducible in-vitro proliferation of cells. This note describes the technical design of a novel, fully automated cell culture system that is "free of tubing". It is based on the HAMILTON MICROLAB® STAR pipetting workstation and has been co-developed by HAMILTON and Life & Brain, Bonn.

Figure 1: *Fully automated cell culture system based on the MICROLAB® STAR platform. The system is housed in a laminar flow hood and serves two external Kendro incubators (4°C/37°C).*

Equipment and Materials

Equipment

HAMILTON Cell Culture System Cell^{host} was validated under GLP and consists of:

- MICROLAB® STAR, 8 channels, 1000µl with built-in robotic plate-handler (iSWAP) and autoload
- HAMILTON plate lifter for media changes
- Kendro incubator Cytomat 6000 for 153 SBS 6-well plates or 189 96-well plates including CO_2 regulation, barcode scanner and 400mm linear track
- Kendro incubator Cytomat 2 C450 for 20 medium containers including CO_2 regulation, barcode scanner and 400mm linear track
- Laminar flow chamber from Bigneat with HEPA and active carbon filters
- CAT SH 25/26 heated shaker for plates, 20mm amplitude max., 50-200/min.

Labware

- 20 medium tubs with lids, autoclavable 300ml max., 200ml working volume

Technical Design

The core of the system is the MICROLAB® STAR pipetting workstation equipped with monitored air displacement pipetting technology. This eliminates use of tubing, pumps or system liquids, thus significantly reducing the risk of contamination by bacterial growth.

An internal robotic hand – the iSWAP – handles SBS standard cell culture plates on the deck. One or two Kendro incubators are fully integrated into the system (fig. 1).

Typical manual processes like plate agitation are perfectly mimicked by analogous robotic movements.

The system is controlled by a standard PC and Hamilton's open and flexible Microlab Vector Software for process control and 3rd party component integration.

Optimized Data Tracking and Task Scheduling

Every operation on the single plates is monitored and tracked by the Cell^{track} data base, enabling complex

Figure 2: *HAMILTON Cell^{task} software enables repetitive task management, e.g. changes of media every n days.*

HAMILTON

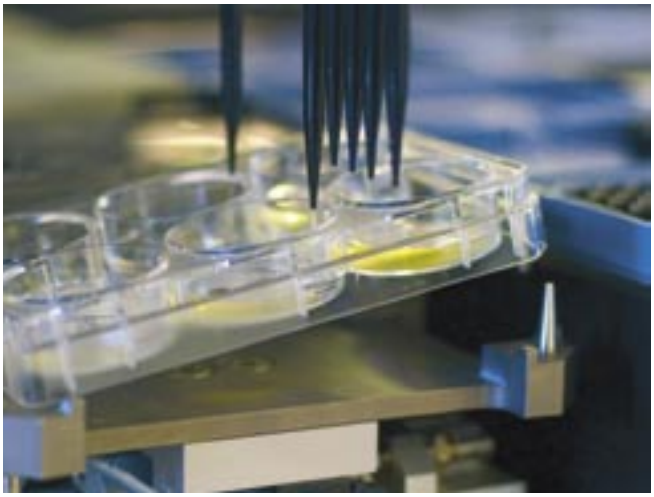

Figure 3: *HAMILTON plate lifter mimics human manipulation of cell culture plates thus facilitating the complete removal of old medium.*

process handling, also under CFR 21 Part 11 regulations. Cell[task] allows scheduling processes, making repetitive tasks easier.

Typical Processes

The typical processes this system is intended for are

- change of media in cell culture plates during pre-scheduled runs
- harvesting of cell cultures after trypsinisation
- plating of cells to establish homogeneous cell growth in wells
- addition of growth factors or pharmacologically active substances to cell cultures

A typical change of medium is carried out in an overnight run as follows:

- the plates of interest are selected by a worklist
- the appropriate amount of medium in containers is calculated and requested from the cold incubator; the medium container is then transferred to a heated position
- the first plate is transferred from the warm incubator to the pipetting station and residual medium is removed (see fig. 3)
- medium is changed using disposable tips or washable steel needles
- the plate is transferred back to the incubator

Biological Validation of the System

The biological feasibility has been validated explicitly with respect to

- viability of cells after pipetting (plating, collecting)
- intact cell layer after changing media
- homogeneous distribution of cells in wells after plating
- absence of cross contamination when working with washable steel needles

Applicability

The cell culture system described here is intended for various cell types including embryonic stem cells. It is open to further automation of other cell lines like CaCo2 and downstream applications such as reporter gene assays.

HAMILTON and Life & Brain have proposed and in part validated a fully automated cell culture system for the standardisation of cell culturing processes featuring reliable and highly reproducible automation. With the automation of cell cultures, a significant reduction of manual workload for pharmaceutical and biotech industries comes into reach.

Technical Specifications

Dimensions: 2.4 m (height), 1.4m (depth) X 3.6m (width)

Processing Times (6-well plates, 2ml medium):

- medium change: 340 secs
- cell harvesting: 1500 secs
- feeder cell prep.: 520 secs
- prep. of ESC plates: 940 secs

System Scalability:

- the modular architecture allows additional deck integration capacity.
- incubator is scalable to 1000 96-well plates
- integration of imaging systems is an additional possibility

LIFE & BRAIN

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