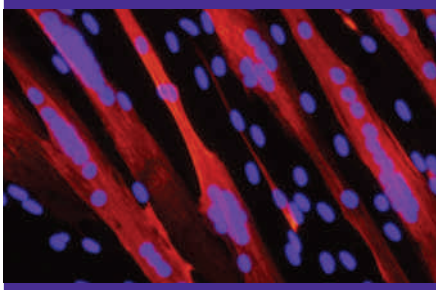


Image supplied by Cook MyoSite Inc.

An assay a day…

The latest in cell based assays

Cell based assays are a quick and cost-effective way to improve the predictability of drug efficacy and toxicity screens by detecting ineffective and potentially toxic compounds early in the drug development process before significant time and resources have been invested. Some of the latest cell based assays and systems as well as new substrates, tools and services are highlighted below.

Assays and kits

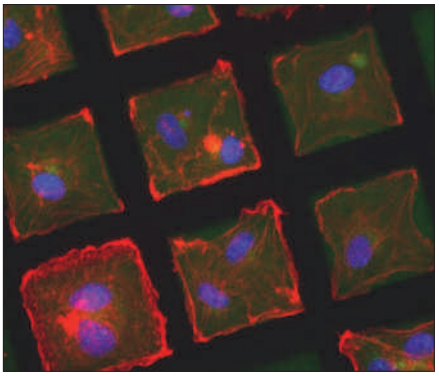
AMS Biotechnology has announced **two new histone deacetylase (HDAC) cell based assay kits** that provide an easy tool for studying the activity and inhibition of the full range of HDAC enzymes (1-11). The new AMSBIO HDAC cell based assay kits provide a fast and fluorescence-based method that eliminates procedures that are often used in traditional HDAC assays i.e. radioactivity, extractions, or chromatography. By using a cell-permeable HDAC substrate in the new assay kits, the activity of various protein lysine-specific deacetylases, including HDAC-containing complexes, can be measured in intact cells in a simple and homogenous manner. The fluorescence of the deacetylated reaction product can be analysed using a plate reader or a fluorometer. In addition, the new assay procedures require only two easy steps, each performed on a single microtitre plate.

QTempo from **InfiniteBio** is a new *in vitro* cardiotoxicity assay technology using stem cell-derived cardiomyocytes developed by ReproCELL in Japan. The QTempo assay directly measures the QT interval in stem cell-derived cardiomyocytes for the assessment of drug induced QT/QTc liability. QTempo closely mimics clinical parameters in an assay that cost-effectively screens early stage development compounds. To increase confidence in the safety of a drug before further development, compounds may be screened under a wide variety of conditions and concentrations. The QTempo assay is available in a variety of formats, which use beating cardiomyocytes derived from either human iPS/ES cells or monkey ES cells. QTempo provides a combination of accuracy and efficiency unmet by other models. It is a perfect tool for verifying hERG assay results, before the time and expense of animal testing.

Cellular Dynamics has introduced **iCell™Cardiomyocytes**, human induced pluripotent stem (iPS) cell-derived cardiomyocytes. These human cardiac cells are specifically designed to aid drug discovery and improve the predictability of drug efficacy and toxicity screens through detection of ineffective and potentially toxic compounds early in the pharmaceutical pipeline process before significant time and resources have been invested. There are several advantages to using iCell Cardiomyocyte's: the cells provide a fully-functional, human-based cardiac model system; they are homogenous and reproducible; and they are easy to implement.

Primary human skeletal muscle derived cells (SkMDC) and complementary products that can be utilised in cell based assays are provided by the "muscle cell experts", **Cook MyoSite Inc.** SkMDC differentiate into multinucleated skeletal myotubes, which could be useful for assays investigating signaling pathways and small molecule drug discovery and toxicity throughout the development of skeletal muscle. SkMDC are isolated consistently, have high purity and viability, and expand reliably while maintaining phenotype. A gene array characterisation is provided with each SkMDC purchase to clearly define the starting culture, which is an industry-first. Cells are categorised on the company's website by

Gentix' CellReporter system



Intelligent Substrates' BioWrite™ protein micropatterns

donor age, gender, and other important donor social/medical information so that the desired cell population can be selected easily by customers each time they order. Cook MyoSite offers several varieties of MyoTonic™ Culture Medium to ensure robust and consistent growth and differentiation of SkMDC.

Systems and services

A significantly enhanced capability for quantification of cellular responses is offered by the **Genetix' CellReporter** system. The multi-application platform is suitable for a wide range of cell based assays such as cell cycle analysis, cytotoxicity studies and protein translocation monitoring. These assays can be used as biological models of physiological situations, for example when investigating the effect of drug candidates on a cancer cell model. CellReporter is supported by flexible image analysis software which identifies and analyses each object, such as the cell nucleus, thereby distinguishing between the responses of individual cells within heterogeneous populations. This means users can optimise and standardise image interpretation for each assay, view cell morphology and check data quality. Thus, using the CellReporter system enables scientists to increase throughput of these assays without compromising image or data quality.

TTP LabTech launched its **new contract screening service** based around the company's HCS technology, the Acumen® microplate cytometer. The service will provide clients with high-content data using cell based assays for the investigation of various biological phenomena - including cell cycle, RNAi profiling, angiogenesis and signal pathway profiling. Initially run from TTP LabTech's headquarters in the UK, the service is currently available in two forms, Standard and Full. The Standard Service offering includes the rapid scanning and analysis of pre-prepared experimental plates, whilst the more extensive Full Service incorporates the entire process from cell culture through compound/reagent treatment, to screening, analysis and data reporting, and can include assay development where required.

Substrates and tools

Intelligent Substrates offers new **BioWrite™ line and grid protein micropatterns** on glass coverslips for cell based applications. The fibronectin patterns have feature sizes ranging from 15 to 100 µm, which by restricting the sites of cellular adhesion, and spreading can define the location, size, and morphology of cultured cells; control cellular functions; direct migration; and minimise variability in cell based assays. Biowrite micropatterned protein substrates have a number of significant benefits over standard substrates: 1) Patterned substrates can increase the sensitivity and lower the variability of cell based assays by constraining cells to defined shapes suitable for cell averaging analysis. 2) The predefined placement of cells on the substrate simplifies automated imaging, image processing, and image analysis. 3) Greater sensitivity, lower variability, and simpler automated image analysis means that researchers will get better results faster. "It is clear that micrometer-scale manipulation of the cellular microenvironment will likely be a foundation of 21st-century biomedical research and cell based applications," said Will Heinz, Ph.D., CEO of Intelligent Substrates.

The **Oris™ Pro Collagen I Cell Invasion Assay** has been added to **Platypus Technologies** cell motility assays product line. The assay uses a non-toxic biocompatible gel (BCG) to form a centrally located and temporary cell-free zone on cell culture surfaces. Cells are seeded into the 96-well plate and attach in a monolayer around the BCG. The BCG dissolves to reveal a Detection Zone and a Collagen I overlay is added to create a 3-D environment for cell invasion into the Detection Zone. This new kit enables researchers to save time and cost by utilising automated liquid handling equipment for fast set-up of high throughput assays. Researchers can capture and quantify real-time cell migration data using microscopes and High Content Screening and High Content Imaging instruments. Cell invasion is measured *in vitro* by the ability of adherent cells to move through a 3-D extracellular matrix (ECM) that mimics an *in vivo* environment. The new assay offers a versatile method that allows for imaging and quantitating cells invading through a 3-D ECM in real-time.

Bangs Laboratories offers polymer and magnetic microspheres that may be used to support cell based assays. Antibodies, peptides, and other ligands may be coated on the company's new **1µm ProMag™ microspheres** to magnetically separate target cell populations and the new **Bind-IT™ pre-activated chemistry** simplifies bead coatings. Submicron fluorescent particles have been employed to analyze the expression and distribution of cell surface markers, with peptide-coated versions used to study intracellular signaling networks.

> **"It is clear that micrometer-scale manipulation of the cellular microenvironment will likely be a foundation of 21st-century biomedical research and cell based applications."**
>
> Will Heinz, Ph.D.
> CEO, Intelligent Substrates

Companies mentioned in this Product Focus:

AMS Biotechnology – www.amsbio.com
Bangs Laboratories – www.bangslabs.com
Cellular Dynamics – www.cellulardynamics.com
Cook MyoSite Inc. – www.cookmyosite.com
Genetix – www.genetix.com
InfiniteBio – www.infinitebio.com
Intelligent Substrates – www.intelligentsubstrates.com
Platypus – www.platypustech.com
TTP LabTech – www.ttplabtech.com

Advertisement feature

Image supplied by GE Healthcare

Tagged out

Label-free and more – advances in HTS

The development of high throughput screening (HTS) has transformed the drug discovery process during the last decade. Recent advances have included the improvement of label-free detection techniques, which offer researchers more flexibility and speed for high throughput screens compared to traditional methods of detection using radioactive or fluorescent tags. Also contributing to the advance of HTS is an increase in the number of screening libraries available to researchers, and innovation in laboratory automation. Some of the latest products are detailed below.

Label-free screening

A powerful solution for large-scale, label-free molecular interaction analysis is available with **GE Healthcare's Biacore™ 4000**. Biacore 4000 delivers high quality binding, kinetic, affinity, concentration, and specificity data in both screening assays and detailed characterisation studies. The system has the capability to analyse up to 4800 interactions in 24 hrs. Biacore 4000 is supported by dedicated software packages for the key drug discovery application areas of small molecule discovery and antibody screening and characterisation, which fully exploit the capabilities of the system. The Antibody Extension Package enables Biacore 4000 users to get the best out of their system for antibody analysis applications, saving time and reagents in biotherapeutic development.

The **RapidFire 300** system for high-throughput screening of *in vitro* ADME assays from **BIOCIUS Life Sciences** enables researchers to perform a wide range of *in vitro* ADME assays with 24-hour, unattended operation. Producing label-free data at six to eight seconds per sample, drug discovery researchers can now use the high throughput, mass spectrometry based method to analyse *in vitro* ADME assays in a fraction of the time required for conventional HPLC mass spectrometry techniques. RapidFire 300 can fully integrate with any manufacturer's triple quadrupole mass spectrometer and provide data compatible with customers' existing laboratory information management systems. "ADME data is critical in all phases of a fully integrated drug development program but data in the lead discovery stage was previously limited by time and labour-intensive screening platforms," said Can "Jon" Özbal, PhD., Vice Chief Operating Officer, BIOCIUS. "RapidFire 300 was developed to meet investigators' demand for high quality *in vitro* ADME data with a short turnaround time."

A high-performance set of screening tools has been launched by **PharmaDiagnostics** to accelerate the drug discovery process for pharmaceutical and biotechnology companies. The **SoPRano™** screening tools use the proven principle of surface plasmon resonance and make it available in high throughput on a standard plate-reader, without the need for costly specialist

Material compiled by College Hill

www.collegehill-lifesciences.com

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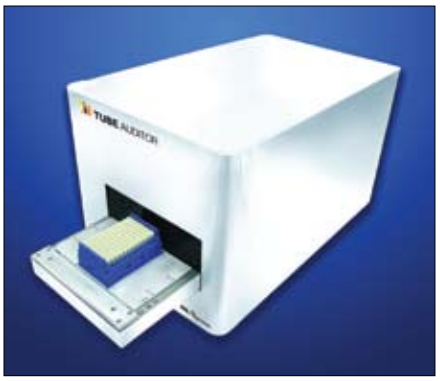
The Capit-All™ IS Automated Capper/Decapper from Thermo Fisher Scientific



RTS Life Science's Tube Auditor

equipment. PharmaDiagnostics' localised surface plasmon resonance technology is broadly enabling, with easy to use protocols, and is applicable to a range of assays for both small molecule and antibody screening and characterisation. "With SoPRano, PharmaDiagnostics is providing label-free screening for a much broader range of researchers," said Dr David Ricketts, CEO at PharmaDiagnostics.

Kits and reagents

Focused collections of receptor ligands, enzyme inhibitors, natural products and FDA approved drugs are available from **Enzo Life Sciences**. **Screen-Well™ libraries** are focused collections of compounds ideal for assay development, receptor de-orphaning, drug repurposing, and lead screening. The libraries are ready-to-screen, with each compound dissolved in DMSO and aliquotted to a 96-well plate, making the Screen-Well libraries ideal for either high content or traditional high-throughput screens. The latest addition to the Screen-Well collection of compounds is an FDA approved library of 640 drugs that have been carefully selected to maximise chemical and pharmacological diversity. It contains clinically-relevant pharmacophores for structure-activity relationship (SAR) or toxicity studies and is ideal for drug repurposing and repositioning programs.

Intelligent Substrates provides a new level of experimental control over cell structure and function with the introduction of **BioWrite™**, a protein micropatterned substrate for cell and tissue culture. BioWrite consists of line and grid micropatterns of the extracellular matrix protein fibronectin on glass coverslips. The patterns have feature sizes of 15 microns to 100 microns, which, by restricting the sites of cellular adhesion and spreading, can define the location, size, and morphology of cultured cells, control cellular functions and minimise variability in high throughput screening applications. This product offers improved sensitivity, lower variability, and simpler automated image analysis.

The **Proteome Profiler *96* Antibody Array**, a new 96-well microplate-based platform for multi-analyte profiling is available from **R&D Systems**. Three Proteome Profiler *96* Phospho-RTK Antibody Arrays are now available, each consisting of microplate wells pre-spotted with a carefully selected panel of capture antibodies. The assay utilises the classic two-site sandwich immunoassay technique and a suitable camera system to detect the relative levels of up to 16 phosphorylated receptor tyrosine kinases in a single sample. Proteome Profiler *96* Antibody Arrays are specially designed to ensure antibody compatibility, high specificity and high sensitivity.

Accessories

Featuring unique vision technology allowing for fast and accurate volume measurement of samples, the **Tube Auditor** from **RTS Life Science** enables measurement of sample volumes and, uniquely, the detection of precipitate in sample tubes. The RTS Tube Auditor is a bench-top instrument suitable for manual operation or integration into automated systems. Its high speed vision technology allows a full 96-way SBS tube rack to be audited in less than 2 minutes. The instrument ensures complete sample safety and avoids the potential for sample degradation as there is no need to de-cap tubes during the auditing process.

In collaboration with **The Automation Partnership**, **Thermo Fisher Scientific** has introduced the new **Capit-All™ IS Automated Capper/Decapper**. This robust, high-throughput instrument can de-cap or re-cap an entire rack of samples in less than ten seconds, while ensuring secure capping by individually sealing each tube, by its own separate clutch mechanism, to the optimal torque. The incorporation of an automated drip tray and a vacuum extraction port reduces any risk of contamination, and the life span of the tubes and caps is significantly increased due to specially molded parts preventing distortion and damage to the caps after repeated use.

TTP LabTech has launched its **Lab2Lab** automated sample transport system, using the proven pneumatic technology at the heart of the comPOUND sample store. Lab2Lab uses a network of uPVC tubing to connect a minimum of two stations – which can be in different rooms, or even on different floors – and allows samples to be transferred using a blast of air. This system can provide on-demand delivery of a single sample tube to a sampling device, then to the analytical hardware, and then to a waste container or collection point. Lab2Lab offers to reduce the time taken for samples to be sent, analysed and returned to the scientist, and optimises the use of expensive analysis instrumentation, as this can be located in a separate core lab to the user.

> **"ADME data is critical in all phases of a fully integrated drug development program but data in the lead discovery stage was previously limited by time and labour-intensive screening platforms."**
>
> Dr Can "Jon" Özbal,
> Vice Chief Operating Officer,
> BIOCIUS Life Sciences

Companies mentioned in this Product Focus:

BIOCIUS Life Sciences – www.biocius.com
Enzo Life Sciences – www.enzolifesciences.com
GE Healthcare – www.gelifesciences.com
Intelligent Substrates – www.intelligentsubstrates.com
PharmaDiagnostics – www.pharmadiagnostics.com
R&D Systems – www.rndsystems.com
RTS Life Science – www.rtslifescience.com
The Automation Partnership – www.automationpartnership.com
Thermo Fisher Scientific – www.thermofisher.com
TTP LabTech – www.ttplabtech.com

Get up and Grow!

Novozymes Biopharma's CellPrime® rAlbumin AF and CellPrime® rTransferrin AF

The cultivation of cells derived from multicellular eukaryotes provides an essential model for studying the activity of cells within an entire organism or in vivo. As mass culture of cell lines is fundamental to the manufacture of viral vaccines and other products of biotechnology, it is vital that best practices and products are invested in at the beginning of any research project to ensure that cell growth and maintenance is approached in the most time and cost-effective way. When compared with the values of cell lines, some of which are irreplaceable, the price of effective media and laboratory equipment is small. Furthermore, the time taken to utilize appropriate techniques is minimal when compared with the time needed to redo unsuccessful experiments. To ensure the most effective protocols for maintaining or growing cells can be easily implemented in any laboratory, a range of innovative cell culture matrices and equipment are available that have been designed to benefit the most demanding research scientists by ensuring the integrity of yields and the validity of research.

Enhanced Growth Performance

R&D Systems new **StemXVivo™ Culture Matrix** is a fully defined proprietary mixture of recombinant human adhesion molecules for the culture of stem or progenitor cells. It is designed to be used as a substitute for basement membrane extract or as a feeder layer in the maintenance and/or differentiation of stem or progenitor cells. StemXVivo Culture Matrix supports normal attachment, growth and marker expression of stem and progenitor cell populations when compared to cells grown on Engelbreth-Holm-Swarm (EHS) basement membrane.

Novozymes Biopharma's range of animal-free recombinant supplements and bioactive proteins have been developed to improve the growth performance of cell lines for viral vaccines. **LONG®R3 insulin-like growth factor-I, LONG® epidermal growth factor, CellPrime® rAlbumin AF and CellPrime® rTransferrin AF** (CellPrime rAlbumin and rTransferrin are sold exclusively through Millipore), have been designed to act both individually and in combination, to enhance the growth performance of vaccine cells in serum-free media formulations. These recombinant bioactive proteins enable the replacement of animal-derived components in the production process, assisting regulatory approval while minimizing risk to product users. The use of bioactive proteins also contributes to greater consistency in process performance and elevates process yields in biopharmaceutical product manufacturing.

Cook Myosite's primary human skeletal muscle-derived cells (SkMDC) are isolated and purified from human skeletal muscle using controlled manufacturing processes developed and refined from over 10 years of research. SkMDC are primitive myogenic progenitor cells that can differentiate into multinucleated skeletal myotubes, which are useful to assay signaling pathways and drug discovery and toxicity throughout skeletal muscle development. SkMDC are consistently isolated and banked with high purity and viability. Cells are categorized online by age, gender and other social/media information so that customers can select the desired cell population each time they order. A gene array characterization is provided with every SkMDC purchase to define the starting culture and by using Cook Myosite's Myotonic Growth Medium, SkMDC can be reliably expanded *in vitro* while maintaining phenotype.

Effective Antibody Production

The new **C5011 hollow fiber bioreactor cartridge** from **FiberCell Systems** is optimized for maximum antibody production when used with the new FiberCell Systems Duet pump. Each cartridge can produce from 20 mg to 100 mg of antibody from a hybridoma cell line every two days in a total volume of 20-40 ml for six months of continuous production or more. The high cell density permits adaptation to FiberCell Systems serum replacement; CDM HD. Used just like serum, CDM HD turns classical media into a chemically defined, protein-free medium optimized for use in hollow fiber bioreactors. The cartridge comes pre-sterilized and is easy to set up, simplifying monoclonal antibody and recombinant protein production. The Duet pump will run two cartridges simultaneously for twice the productivity.

DNA Delivery

Mirus Bio has expanded its transfection reagent portfolio with the development of ***Trans*IT®-2020**, a new high performance transfection solution for broad spectrum plasmid DNA delivery into mammalian cells. TransIT-2020 is suitable for both transient and stable transfection and also works well in typically hard-to-transfect cell types.

Material compiled by The Scott Partnership

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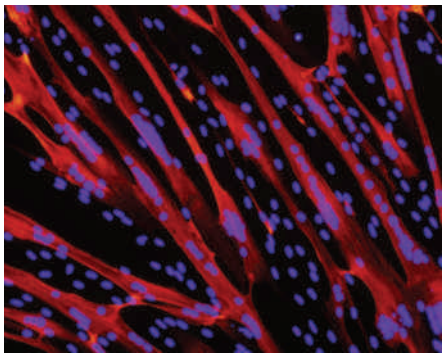

SkMDC from Cook Myosite are banked with high purity and viability

Bioo Scientific's MaxDiscovery Apolipoprotein B (ApoB) ELISA Kit

Milipore's FlowCellect™ kits use flow cytometry for the analysis of cell health

TransIT-2020 is animal-origin free and does not require any culture media change post-transfection, allowing maximum compatibility for all downstream applications.

Maintenance of Cells in Culture

Available in two sizes, the new **triple gas incubators** from **IKS International** offer a high quality culturing environment with excellent temperature accuracy and CO_2 stability. The larger incubator (IVS-9160GC) with 173 liter chamber and eight divided inner doors delivers a good price performance ratio, while the small 33 liter model (IVS-9000GC) with six divided inner doors is ideal for use with lowered oxygen concentrations. Both of the triple gas incubators provide a condensation-free chamber with rounded corners for easy-cleaning and the well-designed interior is fully autoclavable. Very fast recovery times for temperature, CO_2 and O_2 ensure a highly stable environment for embryo growth and an internal HEPA filter prevents contamination. Other features include a dual-beam (non-dispersive) infrared CO_2 sensor and an access port allowing connection to an external XiltriX® sensor for continuous status monitoring.

Analysis of Cultured Cells

The **MaxDiscovery Apolipoprotein B (ApoB) ELISA Kit** from **Bioo Scientific** is a complete, two-step ELISA test that analyzes the quantity of ApoB in tissues, serum, plasma or cultured cells with minimal sample preparation. This kit offers precise protein measurement along with the ability to analyze multiple samples in low-volume, high-throughput experiments. This ELISA is available in 96-well and 384-well formats; both of which have plates that are pre-coated with capture monoclonal antibodies and contain all of the reagents needed to perform the assays. For increased flexibility, the 96-well plate is composed of 8-well breakaway strips.

Millipore has launched **FlowCellect**™ kits for the analysis of cell health using flow cytometry. The kits permit researchers to quickly and easily evaluate mitochondrial health in drug compound screening, apoptosis-related research and understanding the mechanism of diseases. The six new FlowCellect kits include the MitoDamage kit, which provides simultaneous information on mitochondrial perturbations, apoptosis and cell death and the MitoStress kit, which allows study of the inter-relationship between mitochondrial oxidative stress and apoptosis. For researchers who want to further understand mechanistic pathways, Cytochrome C kits allow for evaluation of mitochondrial Cytochrome C levels in apoptotic cells and commitment to the intrinsic pathway of death, thereby simplifying an assay that has been traditionally done with western blots.

Thermo Fisher Scientific has launched the **Thermo Scientific Pierce Agarose ChIP Kit** for fast and reproducible chromatin immunoprecipitation (ChIP) assays. ChIP assays monitor transcription regulation through histone modification or transcription factor-DNA binding interactions. The ChIP technique captures a snapshot of specific protein-DNA interaction as they occur in living cells. The Pierce® Agarose ChIP Assay Kit contains all reagents to perform a successful ChIP assay using mammalian cells or tissue. The specially titrated and tested micrococcal nuclease evenly digests the DNA, eliminating the variability that results from using sonication. The specially blocked ChIP Grade Pierce Protein A/G Plus Agarose Resin provides high binding capacity and low background. The fast procedure uses convenient spin columns for the immunoprecipitation, wash and elution steps, minimizing sample loss.

Live Cell Imaging

Chip-Man Technologies has announced the launch of the **Cell-IQ 2** live cell imaging and analysis system. This innovative platform builds on the success of the original Cell-IQ system, offering fully automated imaging and analysis for the study of live cell behaviour in an optimized stable environment. The Cell-IQ platform allows accurate and reproducible quantitation of results for live cell imaging and has already proven highly successful in a range of laboratory settings. The second generation system provides increased usability and precision for users, offering advanced features for cell biology.

Intelligent Substrates has introduced protein micropatterned substrates for live cell imaging applications. Patterns of extracellular matrix proteins, by restricting the sites of cellular adhesion and spreading, can define the location, size and morphology of cultured cells; direct migration; and control other important cellular functions. Intelligent Substrates' **Substrate Design Center** works with researchers to rapidly develop custom protein micropatterns with features as small as 5 µm on a variety of substrates and formats compatible with common cell dynamics imaging setups. Protein micropatterned substrates can control important cellular functions including mitosis, cell growth, apoptosis, stem-cell differentiation, tissue growth and structure and multi-cell dynamics and interactions. These products and services provide improved sensitivity, lower variability and simpler automated image analysis to enable researchers to achieve better results faster.

Cell Harvesting

Sera Lab has announced the launch of the novel **SplitKits cell dissociation system**, the first specifically designed for use in both serum-based and serum-free methodologies. Developed using a vegetable-based component rather than trypsin, SplitKits avoid any risk of contamination with either animal or human viruses or bacteria and are suitable for a wide variety of cell culture systems. Independent studies conducted in both research and biopharmaceutical laboratories have shown that SplitKits encourage faster cell dissociation than trypsin. Greater control of the dissociation process produces homogenous cell suspensions with minimal batch-to-batch variation. The extremely gentle action of the SplitKits vegetable-based enzyme gives higher cell yields and better cell growth recovery following detachment.

Chip-Man Technologies' Cell-IQ 2 live cell imaging and analysis system.

Companies featured in this product focus:
R&D Systems – www.rndsystems.com
Novozymes Biopharma - www.biopharma.novozymes.com
Cook Myosite Inc – www.cookmyosite.com
FiberCell Systems – www.fibercellsystems.com
Mirus Bio – www.mirusbio.com
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