Seek to discover

Advances in drug screening and discovery

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There are many stages involved in the drug discovery process from target identification and validation through to lead identification and optimisation. The immense pressure that the pharmaceutical and biotechnology industry is under to reduce costs means that all the technologies and processes relevant to drug discovery are under constant scrutiny to find more efficient, accurate and cost-effective approaches. New developments in instrumentation, assays, kits and accessories are described below.

Screening instrumentation

Ion channels play important roles in cell physiology and are ideal drug targets, but their potential has been largely untapped. Traditional manual approaches to patch clamp assays are time-consuming and skill-sensitive. **Fluxion Biosciences** has introduced the **IonFlux-HT** and **IonFlux-16 Automated Patch Clamp Systems** to bring significant gains in throughput, workflow simplicity and affordability to ion channel research. These new systems combine Fluxion's microfluidic technology with integrated electronics to automate the traditional patch clamp assay, the "gold standard" in ion channel research. Ideal applications include primary/secondary screening, lead optimisation and toxicology screening. The IonFlux-HT system includes 64 amplifiers and delivers between 8,000 and 10,000 assays per day using 384-well plates. The IonFlux-16 provides all the features of the HT system with 16 amplifiers, using a 96-well plate format.

GE Healthcare has launched the **IN Cell Analyzer 2000**, a flexible cell imaging system for High Content Analysis with excellent image quality, speed and ease-of-use for all screening and research needs. The flexibility of the system enables scientists to perform a wide variety of previously challenging experiments with a single instrument: from investigative microscopy through to automated screening, and imaging of organelles, cells, tissues and whole organisms. The IN Cell Analyzer 2000 has a unique combination of hardware and software features for extremely fast image acquisition making it ideal for screening. The robust construction of the instrument ensures its reliability for high throughput use when carrying out demanding applications in a multi-user environment. "Combined with intuitive software, as well as expert instrument and applications support, even the most challenging high content assays are now an every day reality," says Leighton Howells, Program Manager at GE Healthcare.

Genetix' Ariol® platform for digital imaging and analysis offers a solution for the quantification of biomarkers in tissue sections and tissue microarrays. Compared with conventional manual reviewing and scoring, Ariol systems drastically reduce review times and have the added advantage of avoiding the errors and operator fatigue that can be associated with manual assessment. The systems produce high quality data and maximise the information captured from every sample. Used in drug discovery and development, preclinical development as well as clinical/translational research and diagnostics, a unique image processing extracts numerical data objectively and consistently. The 'trainable' Ariol Analysis Modules, available for immunohistochemistry, fluorescence, rare events and more general measurements, enable analyses to be optimised according to the specific application. By standardising the entire imaging and analysis process, users are able to base their conclusions on objective, comprehensive data.

Assays, kits and accessories

Because of the vital role cytokines – molecules that stimulate or inhibit the

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Bio-Plex Pro™ cytokine assays from Bio-Rad

Genetix' Ariol® platform for digital imaging and analysis

function of other cells – play in cell signalling, monitoring cytokine levels is vital in drug discovery research. **Bio-Plex Pro**™ magnetic bead-based human and mouse cytokine assays from **Bio-Rad** are multiplex assays that offer fast and accurate performance for the detection of multiple biomarkers in a single experiment, using as little as 12.5 µL of serum, plasma, or other bodily fluids. Magnetic bead-based assays overcome the limitations to automation of conventional polystyrene bead assays, which require manual wash methods. These assays enable magnetic separation when used with the fully automated magnetic bead washer, the Bio-Plex Pro Wash Station, which increases assay reproducibility by eliminating user-to-user variability.

The **Cell Counting Kit-8** (CCK-8) from **Dojindo** is a highly sensitive, nonradioactive colorimetric assay that enables the monitoring of drug cytotoxicity in cell culture. Cytotoxic effect can be monitored by looking at the total production of NADH by dehydrogenase activity of the cells. This kit uses the unique water-soluble tetrazolium salt-8 (WST-8) as an indicator of the cells' dehydrogenase production. The components of the CCK-8 are virtually nontoxic to cells, making continuous assay possible. Dojindo has also recently launched the new Cell Counting Kit-SK (CCK-SK), which has a higher sensitivity. This kit allows for a shorter incubation time than CCK-8 to determine cell viability and is suitable for leukocyte type cells, which produce less NADH.

Hollow fibre bioreactor cartridges from **FiberCell Systems** offer a simple two-compartment set-up for *in vitro* toxicology with higher levels of reproducible control of complex growth, infection, treatment, and sampling regimens. This system permits a highly realistic simulation of *in vivo* drug effects in a dynamically controlled system providing data that more accurately reflects biological responses to pharmacokinetics and pharmacodynamics than other methods. The fully disposable cartridges can be used with antibiotics, anti-viral agents and anti-cancer drugs.

The **ADP-Glo™ Kinase Assay** from **Promega** delivers high sensitivity and can be used with up to 1 mM ATP. The assay measures ADP formation and is suitable for any kinase-substrate combination. ADP-Glo tolerates a wide range of assay conditions and can readily replace existing assay technologies, including radioactivity.

The methylation of proteins, xenobiotic drugs, nucleic acids, and oligosaccharides is known to regulate important cellular events including meiosis, biosynthesis, development, signal transduction, chromatin remodelling, and gene silencing. The most frequent methyl donor for this type of enzymatic modification is S-adenosylmethionine (SAM/AdoMET). The **Assay Designs® Methyltransferase HT Activity Kit** is designed for screening candidate compounds that may alter normal methyltransferase (MT) activity and is suitable for use with all SAM-dependent MTs. This kit includes a high concentration of SAM as a separate component, which provides the flexibility to customise the amount needed for specific MT/substrate systems. This is ideal for driving the kinetics of low turnover enzymes and fine tuning HT screens. MT activity is measured without the need for radiolabelled samples, with both endpoint and kinetic assay options available for highly sensitive fluorometric detection.

SABiosciences' SilenciX Cell Lines are ready-to-use target-specific stably silenced cell lines, which provide robust and reliable cellular models for drug discovery, functional genomics and screening. SilenciX cell lines are created using a replicative pEBV-derived plasmid that remains as independent replicons in human transfected cells, which express shRNAs for a long time leading to stable gene silencing. The use of this vector circumvents the shortcomings resulting from the over expression of siRNA, such as saturation of the endogenous RNA-induced silencing complex (RISC) machinery, and avoids random integrations into the genome.

Services and software

Thermo Fisher Scientific recently released its **Thermo Scientific Watson LIMS** (Laboratory Information Management System) that brings critical time and cost savings to pharmaceutical companies and contract research organisations involved in drug metabolism and pharmacokinetic (DMPK) studies for drug discovery and development. The latest release of Watson LIMS, delivers improved efficiencies and reduced validation time, contributing to time and cost savings and improved time to market. Of the many new features unique to Watson LIMS, key among them is the new functionality in Watson 7.4 that simplifies daily workflow for bioanalytical laboratories by delivering enhanced functionality for incurred sample reanalysis (ISR).

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Leighton Howells,
Program Manager, GE Healthcare

Companies mentioned in this Product Focus:

Assay Designs – www.assaydesigns.com
Bio-Rad – www.bio-rad.com
Dojindo – www.dojindo.com
FiberCell Systems – www.fibercellsystems.com
Fluxion Biosciences – www.fluxionbio.com
GE Healthcare – www.gelifesciences.com
Genetix – www.genetix.com
Promega – www.promega.com
SABiosciences – www.sabiosciences.com
Thermo Fisher Scientific – www.thermo.com