The Only Way is Up

HTS tools that raise the game

Since its dawning in the mid-1990s and following years of development and investment, HTS has become a mainstay of modern research. Compounds originally identified through HTS are now reaching late stage clinical trials and coming to market. At times, the return on investment of HTS has been challenged as the results have not lived up to the hype, but as technology advances, so too does the efficiency, speed and breadth of application of HTS tools. Some of the latest tools are outlined below.

Image supplied by Wheaton Science Products

Assays and Analysis

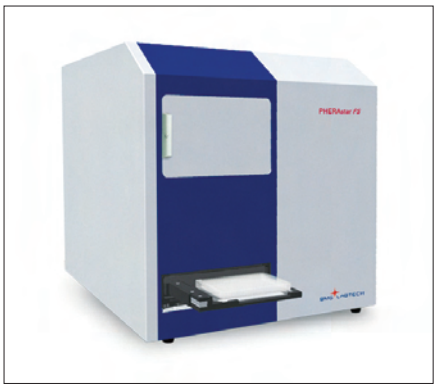
Isothermal Titration Calorimetry (ITC) provides detailed information on the binding forces of compounds to their target macromolecule. This is vital in order to understand the binding mechanism of action, to validate hit compounds and to guide compound optimisation into more potent leads. As modern ITC instrumentation has evolved, these instruments have become more sensitive, faster and easier to use. The new **iTC200** and **Auto-iTC200** systems from **MicroCal** (now part of **GE Healthcare**) have reduced the amount of sample required to obtain a complete binding profile to as little as 10 µg of protein. The Auto-iTC200 system combines the superior performance of the iTC200 with full automation and integrated liquid handling, providing a sample throughput of up to 75 samples per day, with a capacity to run 384 samples unattended. "With the rise in structure-based approaches to drug discovery, it has become increasingly important that biomolecular interactions can be fully characterised. Technologies such as ITC and SPR have gained wide acceptance throughout the world, and are used by major pharmaceutical and biotech companies," commented Steve Spotts, Modality Leader, MicroCal, GE Healthcare.

BellBrook Labs has released the **Transcreener ADP^2 FP Assay**, a new ADP detection assay which offers improved sensitivity and increased flexibility over the original ADP detection assay. Like the first generation Transcreener ADP assay, it allows detection of any enzyme that converts ATP to ADP without the use of coupling enzymes such as luciferase. The assay enables detection and screening of established drug targets including protein and lipid kinases as well as emerging targets such as heat shock proteins and other ATPases. Now with an improved monoclonal antibody that allows more sensitive ADP detection and increases the total assay signal, the Transcreener ADP^2 FP Assay achieves a good assay window using ATP concentrations as low as 100 nM or as high as 1 mM under initial velocity conditions with a $Z' \geq 0.7$.

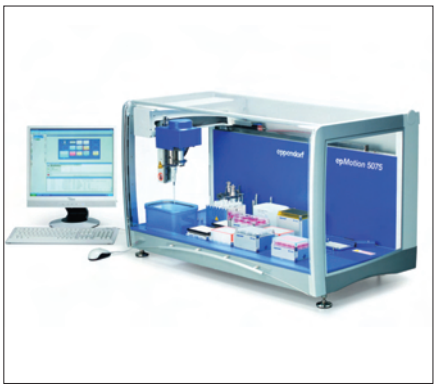
Attagene has launched high-content screening services that employ its **FACTORIAL**™ reporter technology. This technology allows evaluation of the state of gene regulatory networks in eukaryotic cells by profiling the activities of multiple transcription factors with accuracy and reproducibility. The technology comes in two forms: cis-FACTORIAL which surveys the activities of more than 40 transcription factors within cells and trans-FACTORIAL which enables profiling of agonist/antagonist activities of compounds acting on more than 40 human nuclear receptors. The FACTORIAL reporter technology offers a solution for the early stages of drug development, including target discovery, analysis of mechanisms of action, assessment of on-target/off-target activities, and hit-to-lead optimisation.

Detection and Quantification

BMG LABTECH has launched the **PHERAstar FS** multidetection microplate reader, which incorporates several new features. These include Tandem Technology, which uses highly sensitive, filter based detection in all modes and an industry first, ultra-fast UV/Vis Spectrometer; on-board reagent injectors for precise kinetic measurements; advanced bottom reading for cell-based assays; three integrated bar code readers and a dedicated UV-laser for TR-FRET based assays. The PHERAstar FS performs all of the leading non-radioactive detection technologies, including fluorescence intensity, fluorescence polarisation, time-resolved fluorescence/TR-FRET, laser-based AlphaScreen®, luminescence/BRET, and UV/Vis full spectrum absorbance. The PHERAstar FS achieves advanced performance in all reading modes, including HTRF®/TR-FRET, through an innovative



The PHERAstar FS from BMG LABTECH



Eppendorf's epMotion 5075 TMX

lens-based optical system. For HTS automation purposes, the PHERAstar FS is easily integrated into numerous robotic platforms or it can be equipped with BMG LABTECH´s 50 plate Stacker II.

Due to the minimal loss of material, ease-of-use, and quick measurement time, scientists working in higher-throughput environments are beginning to shift away from using traditional fluorescent plate readers for quantitation, and choosing a direct absorbance measurement method such as the **Thermo Fisher NanoDrop™ 8000 Spectrophotometer**. This microvolume instrument allows investigators to perform absorbance spectroscopy with eight 1µl samples simultaneously, greatly reducing the time required to measure 96-well plates of samples. The NanoDrop 8000 allows researchers to work with larger numbers of samples while providing the overall capabilities and ease-of-use of the NanoDrop 1000. The system has been integrated into high-throughput environments such as biorepositories, sequencing labs, and genotyping facilities.

The **RapidFire® System** from **BioTrove** is a mass spectrometry-based, native detection technology for HTS of biochemical assays. Direct quantitative interrogation of a wide range of analytes, including lipids, steroids, prostaglandins and others, enables the HTS of many intractable targets that are not amenable to traditional plate reader-based methods. RapidFire technology provides researchers with a competitive edge by decreasing the time for HTS assay development and the identification of lead compounds. Samples are processed in as little as six to eight seconds per well, orders of magnitude faster than traditional LC-MS technologies.

Accessories

The **epMotion 5075 TMX** from **Eppendorf** features an integrated Thermomixer® to shake and heat or cool sample tubes and plates. As the most flexible of Eppendorf's automated pipetting systems, the epMotion 5075 TMX saves time, reduces costs, and delivers up to 20% higher yields in nucleic acid preparation protocols. Using Eppendorf's ^{2D}Mix-Control™ technology, the Thermomixer's orbital shaking and perfect balance of speed and mixing radius optimises re-suspension of bacteria pellets or beads. Droplets are prevented from collecting on the side of tubes or plate wells, thus eliminating the need for additional centrifugation steps.

Wheaton Science Products has introduced the new **E-Z Ex-Traction®** Glass MicroTubes, which are precision engineered and manufactured to tight tolerances to reduce the chance of failure in automated sample handling and storage systems. The interior wall of the MicroTube transitions smoothly into the conical well at the bottom of the vial, which prevents any loss of material that might get trapped in irregular surfaces and corners. The constant shape and depth of the well enables greater recovery of the sample by automated systems without concern for vial and needle damage. The smooth sides and the patented flat bottom design enable each tube to be 2D bar coded. The finish of the microtubes at the top is straight, not tapered as other glass microtubes on the market, which allows for better sealing of the stopper.

TTP LabTech has developed a bulk dispenser to extend the capabilities of **mosquito®**, its automated nanolitre liquid handler. The new add-on head provides bulk reagent dispensing from eight independent channels to offer assay miniaturisation through precise pipetting of compounds in up to 384-well microplates. With its disposable, positive displacement pipettes that ensure zero cross-contamination and low dead volumes, the bulk dispenser transforms the capabilities of the mosquito's proven nanolitre liquid handling into a highly flexible system for HTS laboratories.

IDT offers high-throughput labs the **HOTplate™** expedited oligo synthesis service. Each HOTplate has 96-wells and is normalised to 2–10 nmoles/well or full synthesis yield. Additionally, all HOTplate oligos are quantitated twice by UV spectrophotometry to certify that they meet IDT's yield guarantee, and mass spectrometry is used to analyse every oligo. For RNAi experiments, IDT offers Dicer-Substrate siRNA (DsiRNA) duplexes. Researchers can also take advantage of IDT's free online suite of oligo design and analysis tools.

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Steve Spotts, Modality Leader, MicroCal, GE Healthcare

Companies mentioned in this Product Focus:

Attagene – www.attagene.com
BellBrook Labs – www.bellbrooklabs.com
BioTrove – www.biotrove.com
BMG LABTECH – www.bmglabtech.com
Eppendorf – www.eppendorf.de
GE Healthcare (MicroCal) – www.microcal.com
Integrated DNA Technologies – www.idtdna.com
Thermo Fisher (NanoDrop) – www.nanodrop.com
TTP LabTech - www.ttplabtech.com
Wheaton Science Products – www.wheatonsci.com