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ELRIG.de forum

Phenotypic Screening und 3D Cellular Screening Models

darmstadtium, 9. März 2017

Sehr geehrte Teilnehmer des ELRIG Forums 2017,

im Namen der ELRIG.de begrüßen wir Sie zum ELRIG Forum 2017 in Darmstadt. Wie bereits in den vergangenen Jahren haben wir mit dem Darmstadtium einen Veranstaltungsort gewählt, der im Herzen von Deutschland, gut erreichbar aus allen Richtungen liegt, und seit jeher mit Wissenschaft und pharmazeutischer Forschung verknüpft ist. Neben August Kékule und Justus Liebig stammt auch Emmanuel Merck aus Darmstadt.

In diesem Jahr sind die Themenschwerpunkte **„Phenotypic Screening und 3D Cellular Screening Models“**. Dieser Schwerpunkt schließt nahtlos an das Vorjahresprogramm „Neue Ansätze im Screening“ an. In den vergangenen Dekaden wurden überwiegend relativ einfache High Content Screenings durchgeführt. Allerdings kamen dabei nicht soviele Kandidaten heraus wie erhofft und von den interessanten Treffern sind viele auf dem Weg zur Zulassung als Medikament auf der Strecke geblieben. Es müssen also neue Wege betreten werden, die Assays müssen die eigentliche Erkrankung besser darstellen.

Um den realen Bedingungen bei der Entstehung von Erkrankungen näher zu kommen, sind 3D-Zellmodelle eine bessere Wahl als Einzelzellmodelle. Schließlich leben Zellen in unserem Körper ebenfalls in dreidimensionalen Organen zusammen. Nur in einem multizellulären Umfeld können manche Zellen überhaupt überleben und ihre natürlichen Funktionen ausüben. In den vergangenen Jahren wurden viele solcher 3D-Zellkulturmodelle entwickelt und kommen zunehmend in der systematischen Wirkstoffsuche zum Einsatz. Diese Entwicklung ist daher ein „Hot Topic“ in der Pharmaindustrie.

Die Generierung physiologisch relevanter *in vitro*-Testsysteme benötigt das Zusammenspiel verschiedener Disziplinen. Daher werden in diesem Forum aktuelle Entwicklungen vorgestellt. Dabei werden die neuesten Ansätze aus der akademischen und der industriellen Forschung diskutiert.

Wir sind sicher, wir haben nicht nur interessante Themen, sondern auch hochwertige Vortragsbeiträge ausgewählt. Wir möchten uns hier schon bei den Sprechern für ihre Vorträge und dem wissenschaftlichen Beirat für die Zusammenstellung des Programms bedanken. Unser Dank gilt auch den vielen Sponsoren, die mit ihrer Teilnahme an der Ausstellung die Kosten für die Veranstaltung tragen und damit dieses Forum erst ermöglichen. Durch dieses Sponsoring-Konzept können wir als ELRIG.de das Konzept realisieren, die Veranstaltungen für alle Teilnehmer kostenfrei zu gestalten und möglichst auch das Catering zu übernehmen. Dieser Rahmen soll es einem breiten Feld an Interessenten ermöglichen, an unseren Forum-Veranstaltungen teilzunehmen und so die Forschungslandschaft in Deutschland und dem deutschsprachiger Raum mit Biotech und Pharmaindustrie anzusprechen.

Die Pausen sind großzügig gestaltet, damit Sie Zeit für die Ausstellung haben und sich mit Kollegen aus anderen Firmen und Gruppen über ihre Erfahrungen und Konzepte unterhalten können. Die ELRIG.de sieht den Aspekt des Networking als wesentlichen Bestandteil des Forums und hofft, dass Sie ihn ausgiebig nutzen.

Interessante Vorträge und gute Gespräche wünschen Ihnen der Vorstand und der wissenschaftliche Beirat des ELRIG.de e.V.

Phenotypic Screening und 3D Cellular Screening Models

TIME		TITLE	SPEAKER	
08:00	08:30	Registration		
08:30	08:35	Welcome by the Chairman of ELRIG.de e.V.	Anthony Zerlin	Elrig.de e.V.
08:35	09:15	3D cell culture for drug development	Ursula Graf-Hausner	Graf3dcellculture, Winterthur, CH
09:15	09:40	Drug screening and profiling in patient derived cultured tissues: towards in vitro (pre)clinical trials	Bram Herpers	OcellO, Leiden, NL
09:40	10:05	Bringing technology to the biology to tackle human, animal and plant health challenges	Paul Andrews	National Phenotypic Screening Centre (NPSC), Univ. of Dundee, GB
10:05	10:15	Snapshot: “Complete Solutions for 3D Cell Culture”	Ute Vespermann	Corning Life Sciences, Amsterdam, NL
10:15	11:00	Coffee break & Poster session		
11:00	11:25	High-throughput biomimetic tissue models	Henriette Lanz	Mimetas, Leiden, NL
11:25	11:50	Drug discovery using kinetic live cell imaging of primary human cells	Enrico Schmidt	Novartis, Basel, CH
11:50	12:15	Cancer metabolism and metabolite-sensing G protein coupled receptors	Claudia Stäubert	University Leipzig, Inst. of Biochemistry, D
12:15	12:25	Snapshot: Five questions to consider before screening your library	Christoph Krüll	Beckman Coulter Life Sciences, Krefeld, D
12:25	13:55	Lunch break & Poster session		
13:55	14:20	The 3rd dimension – bridge between *in vitro* & *in vivo*	Sakshi Garg	Merck, Darmstadt, D
14:20	14:30	Snapshot: Factors to Consider for Designing and Optimizing Assays Applied to 3D Cultures	Axel Johann	Promega, Mannheim, D
14:30	14:55	iPSC-derived neural cultures in 3DProSeed hydrogel well plates	Benjamin Simona	Ectica Technologies, Zürich, CH
14:55	15:20	Label-free biosensor assay to capture holistic G protein-coupled receptor signaling in living cells	Nicole Merten	Uni Bonn, Institut für Pharmazeutische Biologie
15:20	15:30	Snapshot “Cellshare – a Cloud Lab for cell based assays”	Lena Schober	Fraunhofer IPA, Stuttgart, D
15:30	15:50	Coffee break		
15:50	16:15	Screening Methodologies based on Seahorse	Fabiana Perocchi	Gene Center Munich, Ludwig-Maximilians-Uni (LMU), München, D
16:15	16:40	Multi-organ-chip developments: towards a paradigm shift in drug development	Reyk Horland	TissUse, Berlin, D
16:40	16:50	Wrap-Up	Anthony Zerlin	Elrig.de e.V.
16:50		End of Forum 2017		

ABSTRACTS

3D cell culture for drug development

Human three-dimensional (3D) tissue models offer new perspectives as R&D tool for drug development in medicine and pharma. 3D tissue models are used as biologically relevant system for preclinical compound screening and disease research. They help to identify potential toxic liabilities in an early phase of the drug discovery process. Furthermore, they provide an insight into pharmacokinetics, physiology and metabolism, effect of protective agents for combinatorial treatment and a lot more. Organoid-based assays present a novel and potentially high-value de-risking strategy, particularly when generated as iPS cell-derived disease models. In addition, 3D tissue models enable the reduction of animal experiments. Different systems of 3D cell culture technology are established covering a wide range of complexity and application. In scaffold-free microtissue engineering cells produce endogenous extracellular matrix (ECM). Hydrogel-based scaffolds provide natural or synthetic ECM for 3D arrangement and rigid scaffolds like polystyrene or ceramics provide an adhesive biomaterial to enforce 3D. A short comparison of the 3D cell culture formats and few examples will be given as an introduction. The most important issue of 3D cell culture is a reliable biological relevance. Additional new technologies try to enhance the complexity of the 3D models in order to establish organ-like tissues with multi cell-types and physiological functionality. Organ-like tissue models should simulate the high complexity of our body. In order to meet this goal, innovative technologies like 3D bioprinting and microfluidics have to be integrated into the production and maintenance process of tissue models. A few examples of different approaches will be described, especially the 3D bioprinting technology. Bioprinting allows the precise deposition of cells, matrix and other bioactive molecules in 3D space and is therefore expected to mirror the *in vivo* tissue complexity. We developed a bioprinting solution with the following features: i) micro valve-based inkjet printheads for cell jetting and contact printing with needles to print into 96 well plates, ii) a chemically-defined ECM-surrogate BioInk that is print- and cytocompatible, iii) a photopolymerization unit to crosslink the BioInk with UV-LED (365 nm) and iv) a cell mixing unit to avoid cell sedimentation in the print cartridge during printing. For tissue generation one layer of BioInk is printed and polymerized providing a stable support for the subsequent printed cell layer. This process is alternated to produce a multi-layered 3D tissue construct. In a recently finished research project together with 3 industrial partners we developed an *in vitro* tool for drug assessment to treat muscle-related diseases. The idea is to provide an all-in-one solution to produce and analyse printed *in vitro* muscle/tendon tissues in a well plate. The customized 24 well plate harbours two posts in each of the wells. The final goal is to print muscle/tendon precursor cells around and in between the posts to induce tissue formation with tendon around the post and muscle fibers between the posts. First, monocultures of primary human myoblasts and primary rat tenocytes were printed separately in a dumbbell-shape around the posts. After cell differentiation, the myoblasts were stained positive for myosin heavy chain (MHC) and myotubes developed and for tendon the characteristic collagen I-distribution around the cell nuclei was detected. The printed muscle tissue is contracting on electrical stimulation and shows physiological functionality. The development of standardized 3D *in vitro* tissue models combined with read-outs is a prerequisite for the future success of 3D tissues in drug development and substance testing. With the current 3D tissue models established in many labs all over the world we play on the tip of an iceberg. To bring this exciting and promising technology to routine application we have to dig much deeper. Robustness, predictability, complexity versus applicability, cost efficiency, reproducibility and validation will be some of the challenges waiting in the next few years. The competence centre TEDD (Tissue Engineering for Drug Development) promotes this development combining academia, clinicians and industry to bring the 3D cell culture to routine application.

Prof. Dr. Ursula Graf-Hausner, Winterthur, Switzerland, www.zhaw.ch/icbt/tedd

Screening and profiling of cancer therapeutics in primary and stem cell-derived Human 3D Tissues

OcellO develops and uses clinically relevant *in vitro* human tissue models for screening and profiling of small molecules and biologics. Tissues cultured in a natural 3D extracellular matrix environment show improved phenotype, function and gene expression profiles compared to 2D monolayer-cultures or spheroids grown in suspension and therefore represent better models for evaluating the effects of new drugs. The analysis of these tissue models, which use cell lines and patient-derived material, is enabled by ultra-high content 3D image analysis, feature extraction and machine learning methods. As well as providing more sensitive measurements of cell growth and viability compared to biochemical assays, phenotypic profiling of tissues allows the measurement of more complex or subtle biology, such as differentiation, invasion and planar polarity. Analyzing a broad spectrum of phenotypic measurements also enables activity of different signaling pathways to be discriminated and toxic effects to be flagged allowing a better ranking of therapeutic molecules.
This lecture will give an overview of OcellO's 3D screening methodology, the use of patient derived tissues and the application to drug discovery for various cancer types.

Bram Herpers, COO, OcellO B.V., Leiden, The Netherlands

Bringing technology to the biology to tackle human, animal and plant health challenges

The National Phenotypic Screening Centre (NPSC) was created with ~€11M of Scottish government investment and launched in 2015 with labs in three top-tier UK Universities: Dundee, Edinburgh and Oxford. A key aim of the centre is to redress the balance in drug discovery away from target-based approaches by focusing efforts towards advanced phenotypic screening, developing the most physiologically-relevant assays possible, leveraging the latest developments in biology, whether that is human, animal or plant systems. In the human disease space we have formed a consortium open to all Pharma/Biotech called the *Phenomics Discovery Initiative* (PDi) that has Janssen as its founding partner. This precompetitive de-risking partnership is developing and validating a range of disease-relevant assays across a spectrum of therapeutic areas. Projects are developed in-house with our existing expertise-base and also sourced from academics, clinicians and SMEs through open calls to our extensive worldwide networks. Emphasis is on using 3D models, patient material, multicellular tissues, organoids, iPSC-derived models and CRISPR/Cas9, using multi-parametric phenotypic readouts where appropriate. We are also building a similar consortium in crop protection and have buy-in from all the major agrichem companies. NPSC aims to advance the science of phenotypic screening by creating a truly multi-disciplinary environment.

Dr. Paul Andrews, National Phenotypic Screening Centre, University of Dundee, UK

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High-throughput biomimetic tissue models

The challenge in creating better biomimetic models lies in capturing the 3D morphology, heterogeneity and boundary aspects of tissues. Our platform allows for a stratified layering of ECM gels optionally alternated with medium perfusion channels. Multiple lanes could be defined with the help of capillary pressure barriers called phaseguides. Clusters of cells are grown in the ECM matrix to provide a natural 3D tissue environment. Monolayers of cells deposited against the ECM matrix form boundary tissues that develop into tubuli. The 3D environment enables long term culture and differentiation of cell clusters. iPS neurons were grown over two months and showed both induced and spontaneous electrophysiological activity as shown by in chip transfected calcium reporters. Lgr5+ small intestinal organoids developed crypt-villi morphology that is typically associated with gut epithelium. Endothelial and epithelial vessels were co-cultured with pericytes to capture the heterogeneity of organs. Our organ-on-a-chip platform is based on a microtiter plate footprint, harboring 96 culture chambers, and fully compatible with both HCS fluorescent and luminescent readout.

Henriette Lanz, Mimetas, Leiden, NL

Drug discovery using kinetic live cell imaging of primary human cells

Cellular behavior is tightly regulated by multiple pathways both in space and time. Modulation of all cellular mechanisms can therefore not only be achieved by targeted delivery of modulator to various subcellular compartments but also by different timing of the modulator. In classical drug discovery the effect of low molecular weight compounds is frequently tested in endpoint assay which limits the molecular mode of actions. When applied on imaging-based read-out, this strategy allows to un-couple cell-treatment from staining and imaging. This approach however does not cover the whole dynamic range or fails completely if no dynamic range can be defined or if the molecular read out cannot be visualized in an endpoint assay. The clearance of apoptotic cells is a key process both during physiological and pathological processes like early development, cancer progression and resolution of inflammation. Engulfment of apoptotic cells is a highly dynamic process regulated by a complicated network of extra- and intracellular pathways. In order to identify modulators of this process with a broad molecular mode of action, dynamic live cell imaging is required. We have developed a fully automated imaging assay to measure uptake of apoptotic corpses using primary human cells in 1536 multiwell format that allows monitoring the complete dynamic range of the process and identify modulators with a broad molecular mode of action.

Enrico Schmidt, PhD, Novartis, Basel, Switzerland

Cancer metabolism and metabolite-sensing G protein-coupled receptors

Cancer cell metabolism differs from that of most normal proliferating cells which is reflected in certain metabolic features like e.g. an increased rate of aerobic glycolysis, fatty acid synthesis and glutamine consumption. In recent years, G protein-coupled receptors (GPCRs) activated by energy metabolites, like lactate, citric acid cycle intermediates and free fatty acids, have gained attention as potential targets in cancer therapy. Our research focuses on the characte-

rization of those metabolite-sensing GPCRs and their possible role in the regulation of cancer cell metabolism. To get a better understanding of their pharmacology we are using a combination of classical second messenger and dynamic mass redistribution assays. We found that hydroxycarboxylic acid receptor 3 (HCA3), which is activated by the fatty acid oxidation intermediate 3-hydroxyoctanoate, is crucial for breast cancer cells to control their metabolism and proliferation. HCA3 mRNA expression is significantly increased in breast cancer patient samples and detectable in primary human breast cancer patient cells. Liquid Chromatography Mass Spectrometry based analyses of breast cancer cell medium suggests a role for HCA3 in controlling intracellular lipid/fatty acid metabolism. Moreover, GPR84 mRNA expression is increased in breast cancer patient samples. GPR84 is activated by medium chain fatty acids and we found that some fatty acids act as agonists at both receptors, HCA3 and GPR84, but induce differential signaling inside the cell. Further analyses are required to understand how the presence and function of these receptors in cancer cells can be exploited in cancer therapy.

Claudia Stäubert, Inst. für Biochemie, Universität Leipzig

The 3rd dimension – bridge between *in vitro* & *in vivo*

Over the last decades, data has emerged highlighting that conventional 2D cell culture tumor models fail to capture important aspects of tumor physiology such as the delicate microenvironment, cell-cell communication, diffusion and availability of nutrients etc. The predictive value of phenotypic screening, especially in the field of tumor biology, is directly correlated to how closely the chosen assay represents the *in vivo* conditions. With that in mind, we at Merck aim to develop an *in vitro* model that closely mimics the cell physiology and biological characteristics of tumors for drug screening. To do so we use the 3D cell culture system known as cellular spheroids combined with a co-culture system to be able to recapture the tumor microenvironment better. Such a model is advantageous in that it can be scaled up for high content screening, it is robust and as well as highly reproducible. Although simplified, cellular spheroids are a great tool that provide deeper insights into questions pertaining to tumor physiology, particularly tumor metabolism.

Sakshi Garg, Ph.D., Lab Head, Discovery Pharmacology, Merck

iPSC-derived neural cultures in 3DProSeed hydrogel well plates

Hydrogels are widely used as an artificial extracellular matrix to grow neural cells in a three-dimensional (3D) environment. 3D cultures have the advantage of closely recapitulating aspects of the human tissues including the architecture and organization among cells (cell-cell and cell-matrix interactions) and more physiologically relevant diffusion characteristics. In 2014, Kim and co-workers reported in Nature a human neuronal cell culture 3D model in Matrigel [1]. The authors demonstrated that the 3D cell culture conditions promoted neural maturation compared to 2D and observed a dramatic increase in the levels of 4-repeat adult Tau isorforms, which are essential for reconstituting tauopathy *in vitro*. Finally, the authors demonstrated the presence of insoluble extracellular amyloid β deposits, an aspect of the disease that is not recapitulated in conventional 2D cultures because secreted Aβ freely diffuses in a large volume of media and is not confined in

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a matrix surrounding the cells. Overall, adopting 3D neuronal cultures to establish Alzheimer's disease *in vitro* models is a promising strategy to recapitulate the biological relevance of *in vivo* model with the advantage of using cells of human origin.
Culturing cells within hydrogels normally requires their encapsulation in the hydrogel during its formation [2]. The encapsulation process is required because of the very limited penetration in 3D of cells deposited on the surface of a pre-assembled gel. The encapsulation process reduces the throughput of the assay, increases the variability and necessitates the simultaneous seeding of different cell populations in case a co-culture assay is envisaged. To tackle these important limitations in the use of hydrogels for 3D cell culture, we developed hydrogels with an "in-depth surface density gradient" promoting the infiltration in 3D of cells deposited on the hydrogel surface (3DProSeed™ hydrogels) [3]. Here we report a preliminary study of the culture of iPSC-derived neuronal cells in 3DProSeed™, with the long term goal of establishing automation-compatible 3D models for neurodegenerative and neurotoxicology screenings while maintaining the highest level of high-content screening (HCS) workflow integration and automation-compatibility. Neurons seeded on 3DProSeed™ hydrogels rapidly extend the neurites in the 3D gels and are viable for at least 19 days. Preliminary functional assays of the calcium activity demonstrates the formation of functional neuronal networks in 3D. Thanks to the presence of the hydrogel surface gradient it is possible to add different cell populations at different time points. Thus, iPSC-derived astrocytes were sequentially seeded and after only 5 days, astrocytes penetrated the hydrogel in 3D and were found associated with the neurites.
In conclusion, we propose a novel hydrogel platform for the development of assays in neurodegeneration and neurotoxicology in 3D, providing simplicity in use, the highest level of automation compatibility and the enabling power of the sequential seeding for establishment of co-culture systems.

Vincent Milleret[1], Greta Thompson-Steckel[2] and Benjamin Simona, Ectica Technologies AG, Zurich, Switzerland, Laboratory of Biosensors and Bioelectronics, ETH Zurich, Zurich, Switzerland

Label-free biosensor assay to capture holistic G protein-coupled receptor signaling in living cells

It is now well accepted that G protein-coupled receptors (GPCRs) simultaneously engage distinct G proteins leading to the activation of multiple downstream effectors, potentially with different potencies, efficacies and *in vivo* relevance. While traditional second messenger assays are intended to portray precisely the activation of defined signaling cascades, label-free technology platforms capture complex phenotypic cell responses in a G protein-unbiased manner and are therefore ideally suited for investigations of orphan receptors. We took advantage of label-free assays, based on dynamic mass redistribution (DMR) of cellular constituents, to investigate the signaling of GPR17, initially in recombinant cells. This receptor has been proposed as dualistic GPCR responding to cysteinyl-leukotrienes as well as uracil-nucleotides and represents according to genetic studies a negative regulator of oligodendrocyte maturation and myelination. We show that GPR17 is completely insensitive towards the putative endogenous ligands but can reliably be activated with the synthetic small molecule MDL29,951. Application of signaling pathway-specific inhibitors allowed us to attribute obtained holistic DMR responses to the engagement of $G\alpha_i$ and $G\alpha_q$. Due to the high sensitivity of label-free detection, the relevance of these two GPR17-induced G protein pathways could be verified in the endogenous environment

of primary rat oligodendrocytes, identifying $G\alpha_i$ proteins as the major contributor to global activity in these cells. Finally, it has been disclosed that activation of GPR17 with MDL29,951 has a negative impact on the oligodendroglial expression of the myelination marker myelin basic protein which largely depends on $G\alpha_i$ activation, emphasizing the predictive power of label-free technology for the relevance of distinct GPCR pathways in physiological processes.

Nicole Merten, University of Bonn, Institute for Pharmaceutical Biology, Molecular-, Cellular- and Pharmacobiology Section, Nussallee 6, 53115 Bonn, Germany

Multi-Organ-Chip developments: Towards a paradigm shift in drug development

Present *in vitro* and animal tests for drug development do not reliable predict the human outcomes of tested drugs or substances because they are failing to emulate the organ complexity of the human body, leading to high attrition rates in clinical studies. Here, Multi-Organ-Chips provide high potential for the *in vitro* combination of different cell types and organoids to realize a better understanding of their physiological in vivo crosstalk. The expectation is that such tests would predict, for example, toxicity, immunogenicity, ADME profiles and efficacy *in vitro*, reducing and replacing laboratory animal testing and streamlining human clinical trials. The ultimate aim for microphysiological systems in drug development is to recapitulate the various stages of a disease and even understand the stages before the disease is clinically manifested, which may open the way for new treatment paradigms. This talk will present examples of current Multi-Organ combinations and how the advanced knowledge and experience acquired will eventually enable the development of a Body-on-a-chip system. In addition, the question of how to qualify and validate these systems will be addressed.

Reyk Horland, PhD, TissUse, Berlin

Foto: Wissenschafts- und Kongresszentrum Darmstadt GmbH & Co. KG

COMPANY PROFILES

ACQUIFER

ACQUIFER is a division of DITABIS AG

ACQUIFER was formed by researchers out of EMBL and KIT and is now a part of the DITABIS AG in Pforzheim, Germany. DITABIS is specialised in the OEM development and production of imaging systems, lab automation and medical devices. The division ACQUIFER developed and now markets an **Imaging Machine** which is a unique imaging platform designed specifically for working with Zebrafish Embryos and other non-adherent samples. Production line engineered to be robust and reproducible, Imaging machine minimises experimental variability due to the device. To accommodate the large data files generated by HCS and other core facility tools they also developed the **HIVE** for transfer and secure storage of the data sets.

Agilent Technologies

Agilent, Waldbronn

Agilent is a leader in Pharmaceutical, Life Sciences, Diagnostics, and applied markets. The company provides laboratories worldwide with instruments, services, consumables, applications and expertise, enabling customers to gain the insights they seek. Agilent has about 12500 employees globally and had revenues of $4.2 billion in fiscal year 2016.

The comprehensive and trusted portfolio offers the most powerful and reliable solutions for diverse application areas. Backed by the technology leading „Cary“ brand, as well as Agilent‘s worldwide service and support organization, Agilent provides a full range of solutions from routine to research.

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Analytik Jena is a leading provider of high-end analytical measuring technology, of instruments and products in the fields of biotechnology and molecular diagnostics, as well as of high quality liquid handling and automation technologies. Its portfolio includes traditional analytical technology, particularly to measure concentrations of elements and molecules, as well as systems for bioanalytical applications in the Life Science area spanning the highly complex analytic cycle of a sample from sample preparation to detection. Automated high-throughput screening systems for the pharmaceutical sector are also part of this segment’s extensive portfolio. Analytik Jena is part of the Swiss Endress+Hauser Group.

Artel, USA

Artel is the world-leading liquid handling quality assurance expert, specializing in solving liquid handling quality, productivity and compliance challenges for life science laboratories.
Artel recently introduced VMS® (Volume Measurement System) which allows for liquid handling process validation and verification within customer's actual workflow. The system is able to accurately and repeatedly measure the volumes of samples in each a well of a microplate without regard to the nature and colour of the samples or the shape of the well and type of plastic.
The MVS® (Multichannel Verification System) enables users to verify the performance of any single- or multichannel liquid handler, pipettor or dispenser in a single measurement, in less than 5 minutes. MVS provides tip by tip accuracy and precision data even at low volumes (0.01µl – 350µl) and allows for direct comparison between any liquid-handler regardless of make, model or location.

Beckman Coulter, Krefeld

Beckman Coulter, als Teil der Danaher Corporation, ist einer der weltweit führenden Hersteller von Messinstrumenten und Testsassays im Bereich der Life Science und Klinischen Diagnostik. Weltweit beschäftigt das Unternehmen über 10.000 Mitarbeiter, die in über 130 Ländern für Sie im Einsatz sind und unsere mehr als 200.000 Systeme betreuen. Die Produkte unseres Life Science Bereiches sind heutzutage ein unverzichtbarer Bestandteil in der medizinisch-naturwissenschaftlichen Forschung, von der Universität, über diverse Forschungseinrichtungen bis hin zur chemisch-pharmazeutischen Industrie. So sind z.B. die Beckman-Ultrazentrifugen, die Coulter-Durchflusszytometer oder auch die Biomek-Pipettierroboter ein Markenzeichen für Innovation. Aber auch in neuen innovativen Bereichen wie zum Beispiel in der Genomforschung mit dem Next Generation Sequencing oder der Nanotechnologie bietet unser Life Science Bereich neue spannende Lösungen.

BioTek

BioTek Instruments ist weltweit führend in der Entwicklung, Herstellung und dem Vertrieb von innovativen Life Science Geräten. Unsere umfangreiche Produktpalette umfasst neben Cell Imaging Systemen, Mikroplatten-Readern, -Washern und –Dispensern auch vollautomatisierte Inkubatoren, Platten-Stacker und Pipettiersysteme. Diese Geräte unterstützen Innovationen in der Life Science-Forschung durch anwendungsübergreifende, sensitive und kosteneffiziente Analyse von Biomolekülen, biomolekularen Wechselwirkungen sowie zellulären Strukturen und Funktionen. Unser Prinzip "Think Possible" bildet dabei die Grundlage für kreative Ideen, unübertroffenen Kundenservice und originelle Lösungen.

COMPANY PROFILES

The Microplate Reader Company

BMG LABTECH

BMG LABTECH ist spezialisiert auf die Entwicklung und Produktion von multifunktionalen Mikroplatten-Readern. Dank deutscher Qualität und technischem Know-How zählt BMG LABTECH zu den Technologieführern auf seinem Gebiet. Seit über 25 Jahren entwickelt BMG LABTECH innovative Technologien, ausgerichtet auf die Bedürfnisse seiner Kunden im Life-Science-Bereich. Die Produktpalette umfasst Mikroplatten-Reader mit unterschiedlichen, optischen Detektionsmethoden für den Einsatz in Pharma- und Biotechnologie-Unternehmen, Forschungseinrichtungen und Routinelabors. Alle Mikroplatten-Reader werden am Hauptsitz in Ortenberg entwickelt und produziert. Neben Niederlassungen in Australien, Frankreich, Großbritannien, Japan und den USA bieten Vertriebspartner auf der ganzen Welt einen umfassenden Kundensupport zu Produkten und Applikationen.

Cellular Dynamics International

Cellular Dynamics International (CDI), a FUJIFILM company, is a leading developer and supplier of human cells used in basic and translational research, drug discovery, toxicity testing, and regenerative medicine applications. CDI leverages technology that can be used to create induced pluripotent stem cells (iPSCs) and differentiated tissue-specific cells from any individual.

Cenibra, Bramsche, Deutschland

Cenibra focuses on cytometry solutions based on cellular imaging, manufactured by technology leaders in the US, Japan, and Germany. The offer ranges from image based cell counters, primary cell analysers, and population analyses through confocal 2D and 3D cytometry, to ultra-multiplexing ChipCytometry for precious samples from clinical and preclinical trials.

Cisbio Bioassays

Cisbio Bioassays is a global developer of products and technologies used in *in vitro* diagnostics and assay development for drug screening procedures. The company pioneered the field of homogenous fluorescence methodologies via its proprietary technology, HTRF®, a highly sensitive, robust technology for cell based detection:

- GPCRs, binding and functional assays,
- Cell based Biomarkers assays,
- Cellular pathways assays,
- Biotherapeutic and Bioprocess,

and widely used by the pharmaceutical industry for the high throughput screening stage of drug development as well as medium and low throughput stages. In addition, Cisbio Bioassays produces a selection of biological reagents and methods used by pharmaceutical and biotechnology companies, as well as contract research organizations (CROs).
For more information: www.cisbio.com

Corning

Corning Incorporated delivers a comprehensive portfolio of highly respected global brands in life sciences research including Corning, Falcon, Axygen, Gosselin, and Pyrex.
We have been the market leaders in cell culture for over a century and continue to innovate.
The acquisition of Discovery Labware strengthened our market leading surfaces capabilities, coupled with our vessels portfolio, provides unmatched strength for emerging cell culture markets (i.e. 3D Cell Culture).
Corning Life Sciences offers integrated solutions to support life sciences and accelerate drug discovery with products like Advanced Surfaces (incl. Matrigel™), Membrane Inserts, and Spheroid Plates.

Dispendix, Stuttgart

Dispendix offers a new generation of simple and reliable non-contact nanoliter dispensing products. The „Immediate Drop on Demand Technology“, I-DOT, enables dispensing of a large variety of liquids, including but not limited to aqueous solutions, PCR-buffer, DMSO up to 100% as well as living cells. I-DOT is scalable from single samples to high throughput.

COMPANY PROFILES

Essen Bioscience, London, UK

Essen BioScience provides instrumentation, reagents, and analysis software that enable researchers to monitor and quantify a wide variety of cellular processes over time. Our flagship product IncuCyte® enables automated live-cell imaging and real-time data analysis, over hours days and weeks directly inside your incubator. Whether monitoring common cellular processes such as proliferation, viability, and apoptosis or more advanced phenotypes, including cell migration and invasion, T cell killing, ADCC or neurite outgrowth, IncuCyte® yields kinetic data and insight far beyond that achievable with conventional end-point or non-image based approaches. Combine IncuCyte® with our range of IncuCyte™ live cell imaging reagents and protocols for integrated solutions to advanced kinetic cell based assays.

Formulatrix

Formulatrix was established in 2002 to provide protein crystallization automation solutions. Since then, we've started developed the next generation of liquid handlers using microfluidic technology. Headquartered in Bedford, Massachusetts, we supply software and robotic automation solutions to leading pharmaceutical companies and academic research institutions around the world. Our team works tirelessly to provide the best products in the industry with support that is second to none.

GC biotech

GC biotech sources the latest developments in automation and reagents for life science research from around the world. We aim to help you take your research to a higher level. As a specialist in life science automation GC biotech is committed to providing the best application and technical support to their customers.

Greiner Bio-One

Die Greiner Bio-One GmbH aus Frickenhausen ist mit ihren Laborartikeln aus Kunststoff und ihren Diagnostik-Kits ein international führender Technologiepartner für die diagnostische und pharmazeutische Industrie sowie Biotechnologie. Das Zellkulturportfolio von Greiner Bio-One umfasst u. a. innovative Produkte für die 3D-Zellkulturtechnik. Dreidimensionale Zellstrukturen können auf einer zellabweisenden Oberfläche oder unterstützend mithilfe von magnetischen Nanopartikeln generiert werden.

Inscreenex GmbH, Braunschweig

InSCREENeX is a biotechnology company providing all kinds of services for the genetic modification of cells. We offer two complementary technologies:

CI-SCREEN™ – Functional Immortalized Cell Lines

- Primary-like phenotype and unlimited availability
- Bioassays for ADME/Tox-testing
- Choose from our portfolio: Airway epithelial cells, Endothelial cells, Chondrocytes, Fibroblasts, Intestinal epithelial cells, Osteoblasts, etc.
- Customized immortalization within three months

SCREENflex™ - Generation of Stable Recombinant Cell Lines

- Targeted Integration in CHO and HEK293 cells
- Your target gene is stably and consistently expressed
- Rapid turnaround time – cell line establishment within 1 month
- Tailored expression of a target gene at low/medium/high level

On the basis of these technologies, InSCREENeX offers pharmaceutical and biotech companies optimal tools and services to develop new drugs under *in vivo* conditions – adapted to *in vitro* set-ups.

Labcyte Europe, Dublin, Ireland

Labcyte Echo® liquid handling systems use sound to precisely transfer liquids without contact, eliminating the use of pipettes. Labcyte instruments are used throughout the pharmaceutical industry, biotechnology, contract research organizations, and academic institutions. Our customers work across a wide spectrum of scientific research, including drug discovery, genomics, proteomics, diagnostics and personalized medicine.

COMPANY PROFILES

Lab Services, We Simply Accomplish

If you choose Lab Services, you are choosing high-quality, top-level service. For more than 20 years we have made a name for ourselves with it. Always keeping your needs in mind, we offer user-friendly innovations in laboratory automation. Our aim is to supply the whole world with PlateButler® from our home base in Europe, and to live up to our excellent reputation. You are the focus in everything we do. We want to gain an in-depth understanding of your processes. Using our creativity and flexibility we aim to find the solution that fits you best. And if the initial idea doesn't put a smile on your face, we can offer you alternatives. Satisfaction guaranteed!

LiCONiC AG

LiCONiC, the world-leading manufacturer of automated incubators and plate hotels for integration, is the first to succeed making automation of biobanking attractive for a broad community. Complete automation of the sample flow combined with latest refrigeration technologies fulfils highest quality standards. In addition, LiCONiC's biobanking solutions feature outstanding economical advantages and help environmental protection by saving precious energy. More than 4500 products are installed worldwide. LiCONiC has become the European standard for automated repository solutions. Products range from a hundred thousand to several million tube capacity. This at temperatures as low as -80°C and new the -196°C full automated LN2 biobanks. LiCONiC offers their most profound knowledgebase helping you implementing the best solutions for your storage application and helping you to take the right decisions for this long-term investment. Please visit our booth for a free consultation. LiCONiC is a certified company and ISO 9001 compliant. Cooperate member at ESBB. Member at the DIN working group to define guidelines of handling biosamples and biobanks.

Miltenyi

Miltenyi Biotec is a global provider of products and services that advance biomedical research and cellular therapy. Our innovative tools support research at every level, from basic research to translational research to clinical application. Used by scientists and clinicians around the world, our technologies cover techniques of sample preparation, cell isolation, cell sorting, flow cytometry, and cell culture. Our 25 years of expertise spans research areas including immunology, stem cell biology, neuroscience, and cancer. Today, Miltenyi Biotec has more than 1.700 employees in 25 countries – all dedicated to helping researchers and clinicians make a greater impact on science and health.

PELOBiotech

PELOBiotech is a leading specialist for HTS, 3D Cell Screening and Cell Lines. So speed up your Drug and Biologics Development: We offer enhanced solutions of 2D and 3D technologies and our broad portfolio covers Cell Lines, iPS/ESC, PCs, SCs as well as special supplements for tumor stem cells. We specialize in early stage compound validation using 3D spheroid models to measure anti-cancer stem cell activity, from primary HTS screening to secondary validation, hit to lead assessment, lead optimization validation, fresh human tumor validation to *in vivo* efficacy studies. We help you study and advance your therapeutic approach to solid cancers and leukemias, diabetes, cardiovascular diseases and other complex condition. We also offer: Multiplex Assays, choose from Proliferation-Assays, Cell-based Assays, Oncogene & Cell Signalling; Screening Kits (TR-FRET) and targeted research methods; modified Primary Cells & Stem Cells; custom cell line development; Diseased Cell Systems.

PerkinElmer

PerkinElmer is committed to improving the health and safety of people and the environment by delivering the knowledge, expertise and innovative solutions that accelerate the understanding of human and environmental health to better diagnose, treat and prevent disease. Our life science research instrumentation, reagents and software tools encompass core areas of research including genomic analysis, cellular, tissue and *in vivo* imaging, biomarkers, bio therapeutics and targeted small molecule discovery bridging the gap between *in vitro* assays and *in vivo* results towards the goal of personalized medicine. Latest highlights from PerkinElmer's product portfolio are **multicolour IHC** detection (up to 7 colours), new development of **high content screening instruments** (Operetta and Opera Phenix), readers with additional Label Free and Imaging capacity and many new wash free **ELISA alternative** and signalling pathway analysis kits based on our Alpha and Lance technology, as well as plates for Imaging and **3D cell culture**.
Find out more about PerkinElmer's solutions at www.perkinelmer.com/lifesciences

COMPANY PROFILES

Promega, Mannheim

Promega zählt mit über 1.400 Mitarbeitern zu den fünf großen weltweit tätigen Life Science Research-Unternehmen. Das 1978 in Madison, WI, USA gegründete, konzernunabhängige Unternehmen stellt Produkte und Systemlösungen für die Gen-, Protein- und Zellanalyse her. Mit diesen lassen sich komplexe biologische Systeme einfach erforschen. Kunden von Promega sind Forschungsinstitute und -zentren, Universitäten, pharmazeutisch und biotechnologisch forschende Unternehmen, Dienstleistungslabors und Behörden. Sie setzen Promega-Produkte in der Grundlagenforschung, bei der Medikamentenentwicklung, molekularen Diagnostik und Identifizierung des menschlichen Erbguts ein. Promega-Produkte können weltweit über 16 Vertriebsfilialen und über 50 Distributoren bezogen bzw. über die Promega Website bestellt werden.

Tecan

Tecan (www.tecan.com) ist ein weltweit führender Anbieter von Laborinstrumenten und Lösungen für die Branchen Biopharma, Forensik und Klinische Diagnostik. Das Unternehmen ist auf Entwicklung, Herstellung und Vertrieb von Automatisierungslösungen für Laboratorien im Life-Science-Bereich spezialisiert. Die Kunden von Tecan sind Pharma- und Biotechnologieunternehmen, Forschungsabteilungen von Universitäten sowie forensische und diagnostische Laboratorien. Als Originalgerätehersteller (OEM) ist Tecan auch führend in der Entwicklung und Herstellung von OEM-Instrumenten und Komponenten, die vom jeweiligen Partnerunternehmen vertrieben werden. Tecan wurde 1980 in der Schweiz gegründet. Das Unternehmen verfügt über Produktions-, Forschungs- und Entwicklungsstätten in Europa und in Nordamerika. In 52 Ländern unterhält es ein Vertriebs- und Servicenetz. Im Jahr 2015 erzielte Tecan einen Umsatz von CHF 440 Mio. (USD 459 Mio.; EUR 411 Mio.). Die Namenaktien der Tecan Group werden an der SIX Swiss Exchange gehandelt (TECN; ISIN CH0012100191).

Foto: Wissenschafts- und Kongresszentrum Darmstadt GmbH & Co. KG

Titian Software, London, UK

Founded in 1999, Titian Software supplies software and consultancy services to improve sample management (of compounds, reagents and biologics) for client's vital life science research. Mosaic is Titian's customizable, modular software product to control and monitor all aspects of sample storage and preparation. Companies worldwide, from small biotech to global pharma, trust Mosaic to provide a seamless, error-free sample supply chain. SampleBank and Freezer Management provide optimized and pre-configured subsets of Mosaic available for rapid deployment.

TTP Labtech

TTP Labtech designs and manufactures robust, reliable and easy-to-use solutions for sample management, liquid handling and multiplexed detection in drug discovery. We enable life scientists through collaboration, deep application knowledge and leading engineering to accelerate research and make a difference together. Our essential tools include state-of-the-art solutions developed for:

- high throughput compound and biologics screening (acumen® Cellista, mirrorball® and fully validated consumables such as sol-R™ beads and plates),
- flexible sample management workflows from ambient to -80°C (comPOUND®, arktic®, lab2lab),
- and unique low-volume liquid handling for genomics, compound screening and protein crystallography (mosquito® X1, mosquito® HTS, mosquito® Crystal, mosquito® LCP, mosquito® HV, dragonfly® and a full range of validated consumables such as tips and plates).

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Phenotypic Screening und 3D Cellular Screening Models

Foto: Wissenschafts- und Kongresszentrum Darmstadt GmbH & Co. KG

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