# Personalized medicine – *in vitro* drug testing on primary cancer cells.

eBook

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Personalized treatments have the greatest potential to benefit cancer patients. Guided selection of the most suitable drug or combination of drugs for a specific patient's cancer profile and genetics avoids a trial-and-error treatment strategy and minimizes collateral effects.

In this context, many university hospitals house dedicated research groups to screen small, dedicated drug libraries on primary tumor cells derived from patient biopsies to match potential treatments to different cancer types. In doing so, researchers gain a better understanding of tumor biology and development that help develop novel therapeutic approaches.

In this eBook we have compiled examples of such laboratories working in the area of pediatric oncology with a focus on leukemias or brain tumors. They all share a reliance on miniaturization and fast processing times to screen hundreds of compounds on very limited and precious patient material.

# Challenges and opportunities in drug screening with primary cells.

With the advent of technologies like NGS, researchers discovered that cancer cells in a human continue to mutate and split into sub-populations with different sets of mutations. One strategy under development to tackle these diverse cancer populations is to use biopsy material from patients to screen in vitro small libraries of approved drugs or late-phase candidates and identify the ones that elicit the best response.

Strategies and methods are typically very agile in an academic research environment and employing full automation for such an approach is not always the best tool. Using a semi-automated approach with benchtop instruments, all dedicated to a single step in the process, can be a more flexible setup.

A key challenge is the low amount of cell material available. Miniaturization is essential to test as many drugs as possible. The laboratories exemplified in the articles below use 384-well and 1.536-well plates, which makes manual processing virtually impossible. Instead, they employ dedicated instruments for cell seeding, compound addition and readout for these high-density plate formats.

Compound addition is the most critical step. Hundreds of wells must be dosed with individual concentrations for a single biopsy sample. Manual serial dilution and dose pipetting into the assay plates is time-consuming and error prone, especially in plate formats beyond 96 wells. Combinatorial setups where several drugs are dosed per well to study synergistic effects cannot be handled manually, requiring dedicated instrumentation to ensure reliable execution.

The fast and simple readout of luminescence-based viability assays are scaled up by performing analyses on microplate readers with a stacker option, each batch of plates representing one copy of the compound library. More recently, however, the higher granularity of data obtained from fluorescence imaging has increasingly pushed this form of cell analysis into the spotlight.

The articles and webinars below feature laboratories using benchtop instruments from Tecan to run these drug screens. The D300e Digital Dispenser is a cornerstone in such a setup, enabling fast and reliable drug dispensing into plate formats of up to 1,536 wells. The Spark® multimode microplate reader and the Spark® Cyto multimode reader with fluorescence imaging offer the necessary readout capabilities.

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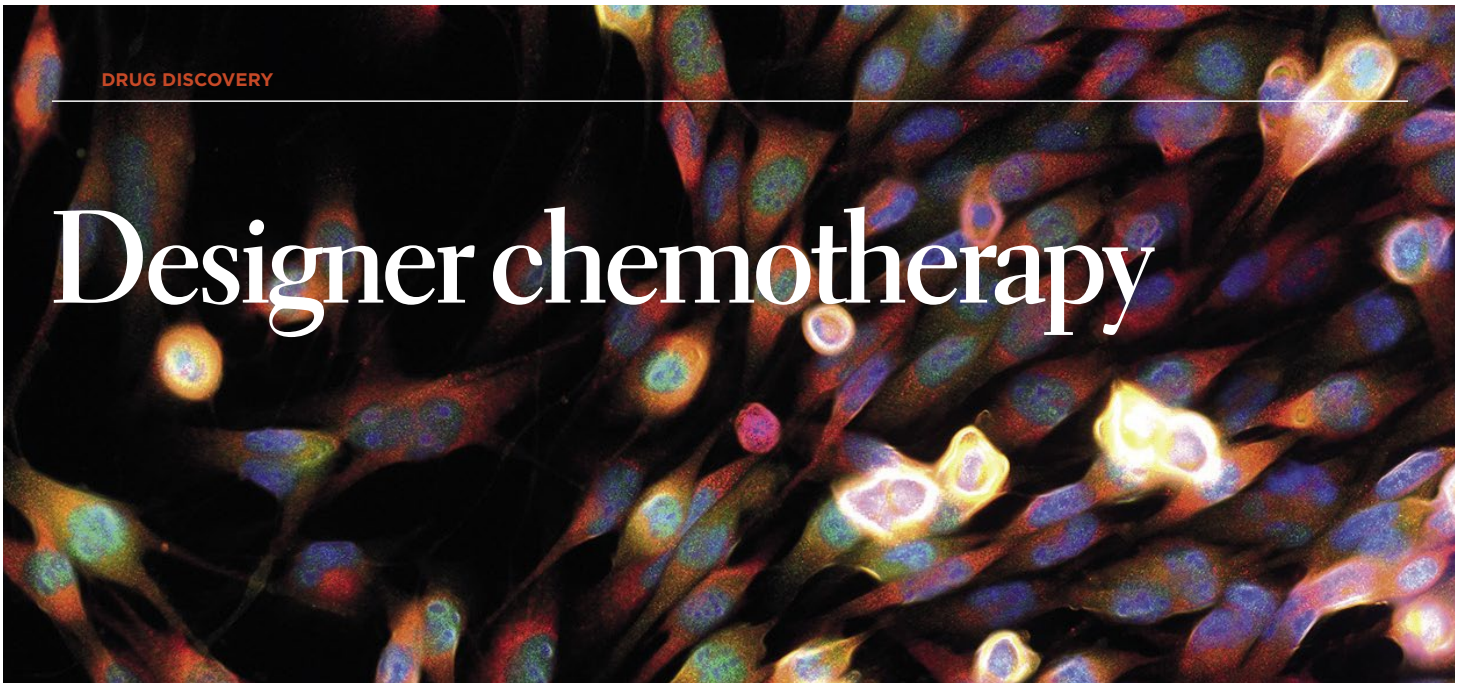


DRUG DISCOVERY

# Designer chemotherapy

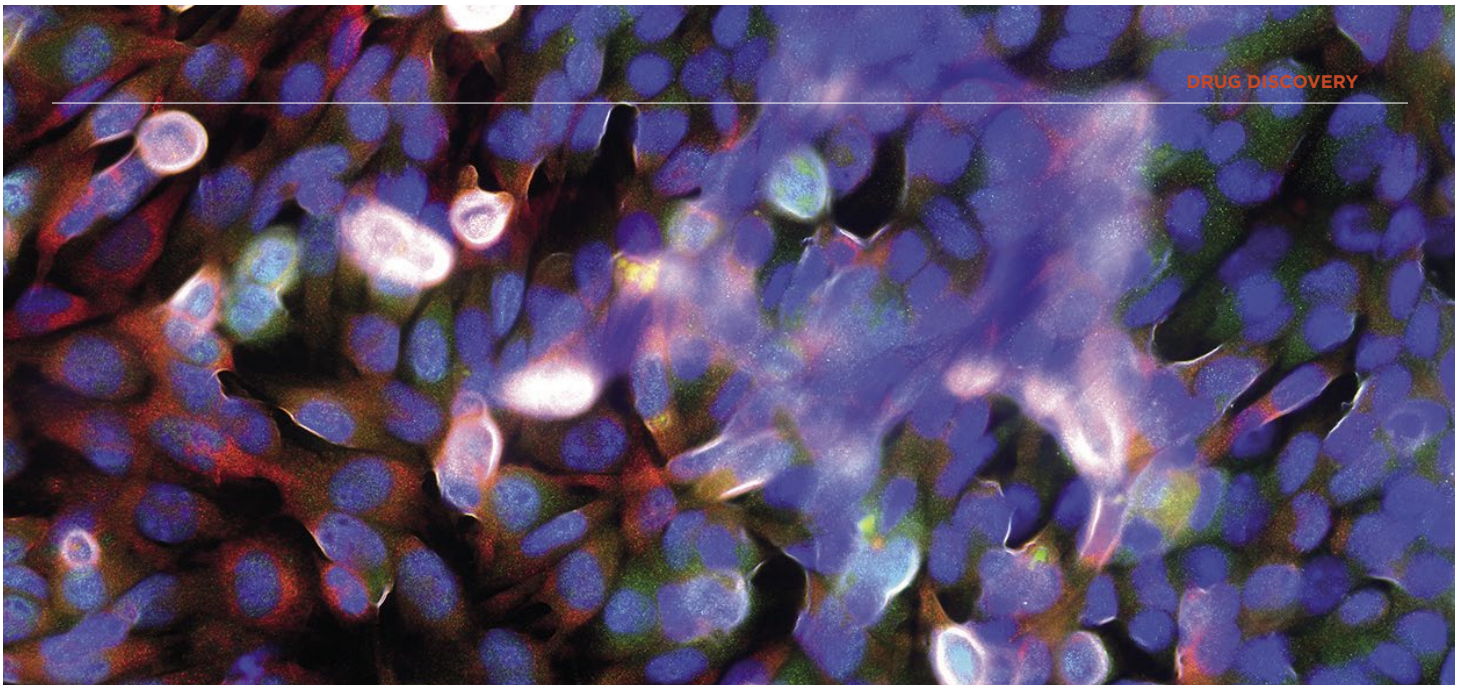
**Brain tumors are the most common cause of mortality in childhood cancer patients, and treatment options are limited, especially for recurrent cases. Researchers at the University Hospital Düsseldorf are using automation to develop a more personalized approach to cancer medicine, performing rapid drug screening to identify novel therapeutic strategies to improve the chances of survival.**

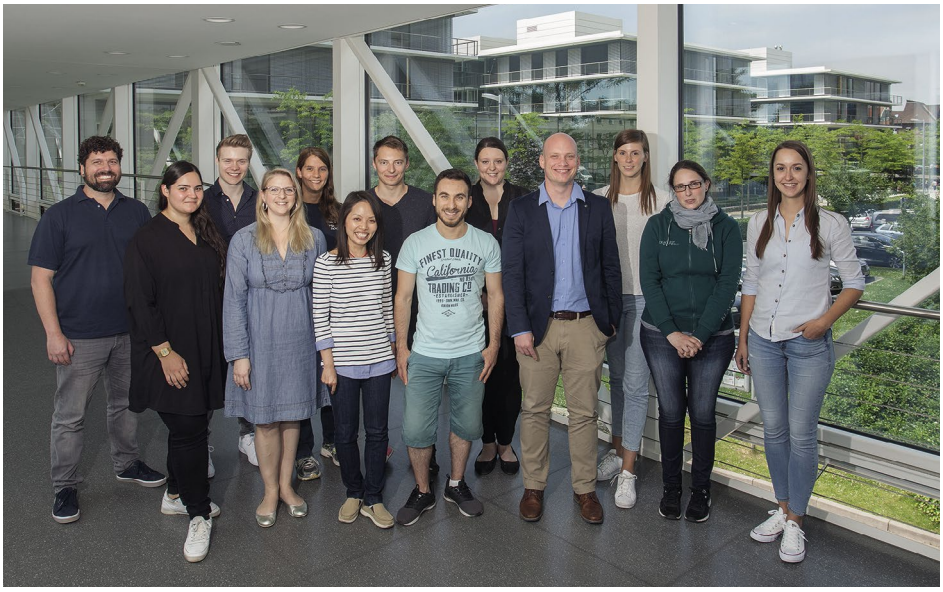
Understanding of the underlying biology and causes of tumor development is critical to advancing treatments and improving mortality rates. Researchers at the University Hospital Düsseldorf are taking a holistic approach to this difficult area of oncology, combining genetic and epigenetic research with proteomics and drug screening. Daniel Picard, Senior Scientist in the Pediatric Neuro-Oncogenomics department, explained: "Our main goal is to characterize tumor-specific alterations affecting the coding and non-coding genome to refine existing or develop novel treatment strategies. Our research focus is the epigenetics of pediatric brain tumors – DNA methylation, microRNAs, and long non-coding RNA – and we combine this work with other approaches to personalize therapies."

"We have a number of drug libraries that we use to screen brain tumor cultures, looking for tailored therapies that could be effective against individual tumors. The library that we are most interested in – which was developed by one of our team members – is comprised of 200 of the most promising compounds that are currently being used clinically or are in phase III clinical trials, and we need about two million cells for this screen. We now have a second, more extensive library that contains around 650 clinically-established compounds, which provides a more comprehensive drug response profile. We then use bioinformatics tools to determine distinct drug classes or molecular targets of interest. We try to manipulate the biopsy-derived cultures as little as possible, to make sure they are similar to the original tumor. Once we have harvested enough cells, we plate out and screen the tumor cells, using an in-house algorithm to determine $IC_{50}$ values. This data allows us to identify which drugs are most effective against that individual tumor model. After screening, we also perform high resolution DNA methylation analysis on both the tumor biopsy and the cultured cells, to identify any methylation differences between the two. They are usually very similar, and that gives us confidence that our screening results are faithfully capturing the expected drug responses in patients."

"When our lab was first set up in 2015, we were going to perform the whole workflow manually in a 96-well plate, but it was clear that automation would reduce our material consumption and increase productivity. We invested in a D300e Digital Dispenser, allowing us to dispense nine dilutions of each of the drugs from our libraries into plates prior to drug screening. We print between 60 and 80 copies of our libraries per run – helping to minimize the potential for batch effects and allowing us to investigate several tumor models at the same time. It's also very cost effective, as we use a fraction of the materials that we would consume if we were conducting everything manually. Originally, we were using 384-well plates but, more recently, we have begun using 1,536-well plates instead, which has turned out to be incredibly useful. We performed several comparison studies to make sure swapping formats didn't affect our results, and the correlation scores were very high, proving just how reliable and consistent the platform is – it's amazing."

"We then use a Spark® multimode microplate reader to monitor the effects of the library compounds using a CellTiter-Glo® Luminescent Cell Viability Assay (Promega). We have a Spark-Stack™ plate stacker which automates our plate loading, so we can just set everything up and walk away – it's so convenient. It's also much more consistent and reliable than our previous equipment – improving the reliability of our data – and it's straightforward to set up and use. We have an amazing team working on the drug pipeline, most of them medical students coming through the lab. Although the majority of them have





The Pediatric Neuro-Oncogenomics department at the University Hospital Düsseldorf

> “The correlation scores were very high, proving just how reliable and consistent the platform is – it’s amazing.”

never touched a pipette before, they are able to use the equipment after a short tutorial. David Pauck, one of our medical students, even developed the algorithm we use to generate our $IC_{50}$ values, which takes the raw data straight from the reader. This has been invaluable, and emphasizes how user friendly the platform is. It’s a real team effort.”

“The automation solutions from Tecan are amazing; they are extremely consistent and help us to generate results that we have confidence in, while reducing our material consumption and saving us countless time. This allows us to focus on our goal of translating our research into a clinical application,” concluded Daniel.

**To find out more about Tecan’s D300e Digital Dispenser, visit www.tecan.com/D300e**

**To find out more about Tecan’s Spark multimode reader, visit www.tecan.com/spark**

**To learn more about the work of the Pediatric Neuro-Oncogenomics group, go to www.uniklinik-duesseldorf.de/unternehmen/kliniken/klinik-fuer-kinder-onkologie-haematologie-und-klinische-immunologie/forschungsbereiche/paed-neuroonkologie**

# Accelerating results from bench to bedside

The direct digital dispensing capabilities of the HP D300 are helping to identify potential new treatments for acute lymphoblastic leukemia at University Children's Hospital Zurich. By enabling picoliter drug volumes to be dispensed straight into cell-based assay plates, the system is helping researchers to rapidly test novel drug combinations directly in patient-derived leukemia cells.

UNIVERSITY CHILDREN'S HOSPITAL ZURICH
*Children's Research Center CRC*

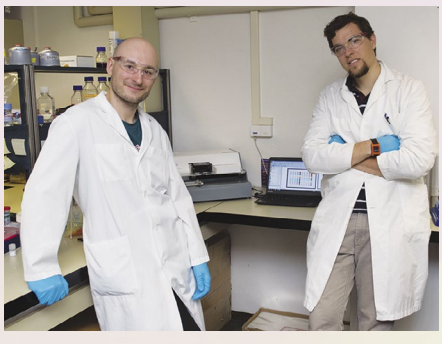
The Division of Pediatric Oncology at University Children's Hospital Zurich (Kinderspital Zürich), Switzerland, has an active translational research program, working in close collaboration with the University of Zurich and other institutes to identify potential new treatments for a number of childhood cancers. As the most frequent form of childhood leukemia, acute lymphoblastic leukemia (ALL) is a key area of research, and the hospital has a special interest in drug-resistant ALL, using a combination of cell-based assays and mouse models to identify novel therapeutic strategies. Dr Jean-Pierre Bourquin, Associate Medical Director of Oncology at the hospital, explained: "We have built a model system that allows us to test material from selected clinically-relevant patients against new drugs and drug combinations. We use a mouse xenograft technique – implanting patient-derived leukemia cells into a tolerant mouse system – to both generate cells for microplate-based co-culture assays and to provide an *in vivo* model. This approach ensures we have enough material to do large-scale investigations which are directly relevant to our patients."

"Due to the drug-resistant nature of the ALL samples we use, we do a lot of drug combination studies, and perform all our cell-based assays in 384-well plates. Designing and pipetting these studies in such high density formats manually can be very time consuming and, like any manual activity, can be prone to errors and inter-operator variability, and so we were looking for ways to improve and streamline our workflow. Automation was an obvious option but, because we are only a small satellite laboratory without the resources and support of a major university facility, a large liquid handling workstation was not a viable option. We discussed our needs with our local Tecan representative, who suggested the HP D300 Digital Dispenser. This instrument is ideal for us; it doesn't take up much space, it's cost effective, and it's very easy to use."

"The D300 is also very convenient for our drug combination studies, allowing us to rapidly design and plan experiments simply by entering the relevant parameters into a matrix. The system then randomizes the plate layout and dispenses the correct volumes of each compound directly into the microplate wells. It's incredibly fast and so simple; what would take half an hour by hand is done in just a few minutes. This is a huge advantage when handling human-derived cells, as they spend as little time as possible outside of the incubator."

"The speed of the instrument is also of potential clinical importance, as we are currently exploring using it for drug activity profiling as part of a clinical trial for pediatric patients whose leukemias do not respond to the standard treatments. These patients are offered highly accelerated whole genome investigations and, at the same time, we profile the activity of a selection of compounds for compassionate use 'salvage' treatments. In this situation, the speed and reproducibility offered by the D300 is obviously a real benefit."

"For example, in a recently published study[1], we used this approach to help us investigate the drug susceptibility of a very rare TCF3-HLF-positive ALL characterized by a chromosomal translocation. Using the D300, we were able to investigate the sensitivity of this ALL to venetoclax – a drug more commonly used in chronic leukemias – in combination with a range of other therapeutics. The data from this study was very promising, and we are now investigating these combinations using the *in vivo* mouse model, with outstanding results."



Viktoras Frismantas and Dr Scott McComb with the hospital's D300 instrument

"The introduction of the D300 has been a big improvement for our workflow, proving the ideal complement to the equipment we already had in the lab. It has enabled us to substantially accelerate many experiments, exploring more complex drug combinations and asking more focused questions. We mostly work with small molecules in DMSO, but the recent upgrades to the D300 mean that we now also have the ability to dispense aqueous solutions, allowing us to investigate biological agents, such as antibodies and antibody-derived therapeutics. Ultimately, the system is helping us to take a more personalized approach to the management of this rare population of patients with highly resistant disease."

"This instrument is ideal for us; it doesn't take up much space, it's cost effective, and it's very easy to use."

To find out more about Tecan's D300e, visit **www.tecan.com/d300e**

To learn more about University Children's Hospital Zurich, go to **www.kispi.uzh.ch**

1) Fischer, U *et al.* Genomics and drug profiling of fatal TCF3-HLF–positive acute lymphoblastic leukemia identifies recurrent mutation patterns and therapeutic options. *Nature Genetics*, 2015, **47**, 1020-1029.

# Working towards cancer-free childhoods

**Developing cancer drugs for clinical trials involves not only identifying and evaluating suitable agents, but also observing how they interact with the cocktail of other drugs in a cancer treatment regime. For the Telethon Kids Cancer Centre in Perth, Western Australia, increasing throughput and reducing assay volumes are essential to save money and time in the race to beat cancer.**

The Telethon Kids Cancer Centre (TKCC) brings together a dedicated group of researchers and clinicians from across the globe to work collaboratively towards developing more effective cures to treat childhood cancer. Brain tumors are the most common form of solid tumor in children, affecting 200 children in Australia each year, and many more worldwide. Within the TKCC, the Brain Tumour Research Program (BTRP) – headed up by Dr Nick Gottardo and Dr Raelene Endersby – is striving to improve patient survival rates and quality of life, through basic and preclinical research, with a key focus on providing the necessary evidence to help a therapy transition to clinical trials.

The TKCC is home to a diverse range of researchers from academia and industry, as well as clinical oncologists, neurosurgeons, radiologists, chemists, pharmacologists and bioinformaticians. It has a close connection with oncologists at the Princess Margaret Hospital – the only children's hospital in the state – and this relationship is key to defining the direction of its research, based on the lack of treatment options currently available to patients. The aim is to uncover more targeted, less DNA-damaging treatments to tackle the tumors.

Raelene explained: "My lab is interested in looking for agents that sensitize cancer cells to conventional treatments, such as chemo- and radiation therapy, and then evaluating them for safety and efficacy. We generate *in vitro* and *in vivo* models of pediatric brain cancer using surgical specimens or genetically modified mice, and then use those tumor cells for drug screening and preclinical testing such as drug sensitivity assays, diluting drugs from high to low concentrations to identify effective doses. What's important for us is looking at how different drugs interact with each other; if we were to put a new drug into an existing protocol, would the drug interfere with the current treatment?"

Three years ago, the team looked to develop the automation in its workflow, to help carry out the thousands of necessary drug tests. Raelene continued: "We were doing lots of dilutions, and serial dilutions, which we were carrying out either manually, or using a much slower robot. When we found out about the D300e, it was a lightbulb moment. This instrument has transformed the activities of our lab. Previously, working together with a colleague, you could generate a small number of plates working solidly for three to four hours. With automation, our throughput went through the roof and increased by four or five times; we are now able to generate faster and more consistent results. Working manually, we would often see a lot more inter-experiment variability than we now do with the D300e, where all of the data overlays beautifully. The error bars are much smaller compared with our previous data, and the increased reliability means that we don't need to repeat the experiment as many times."

Left to right: BTRP team members Tracy Seymour, Hetal Dholaria, Stacey Fazio, Brooke Strowger, Raelene Endersby, Mathew Ancliffe, Hilary Hii and Jacqueline Whitehouse

Dr Jacqueline Whitehouse, senior scientist in the BTRP, agreed: "What would take hours on our previous liquid handling robot, now takes minutes on the Tecan system. The fact that we can use small picoliter volumes also saves money, as some of the novel anticancer drugs are quite expensive and hard to synthesize. Using manual pipetting or our previous robot, we could only work with a minimum volume of about five microliters. We would be wasting a lot of drugs just by the nature of the pipettors and their accuracy, whereas we can now dispense picoliter volumes consistently. We were skeptical at first, but were pleasantly surprised when we were still seeing effects of our drugs on cells using such small volumes. The other advantage is its size, it's so small that it can easily fit inside a biosafety cabinet. This is important for both our precious cultured cells – minimizing the risk of contamination – and for the user, protecting them from exposure to potentially hazardous or toxic novel chemotherapeutics."

"It's very easy and quick to set up; you just copy and paste your data from Excel®. It's been simple to train people and there's not much people can do to break it; the leukemia group within the TKCC is also using our system and it's a good instrument to share with people knowing that it will come back in one piece. We've used it pretty heavily for the past two years and, since there are not many moving parts, it's been great," Jacqueline concluded.

All Tecan products mentioned are for research use only. Not for use in clinical diagnostics.

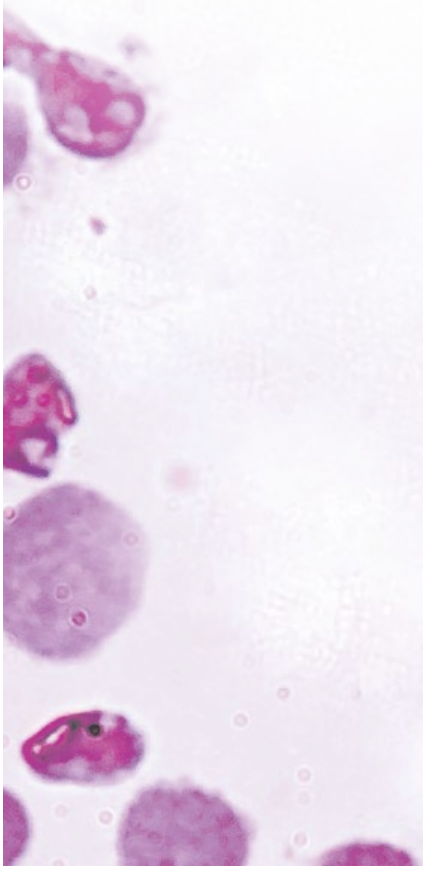
> "With automation, our throughput went through the roof... we are now able to generate faster and more consistent results."

**To find out more about Tecan's liquid handling and automation solutions, visit**
**www.tecan.com/mdx**

**To learn more about Telethon Kids, visit**
**www.telethonkids.org.au**

# Making big discoveries accessible to all laboratories

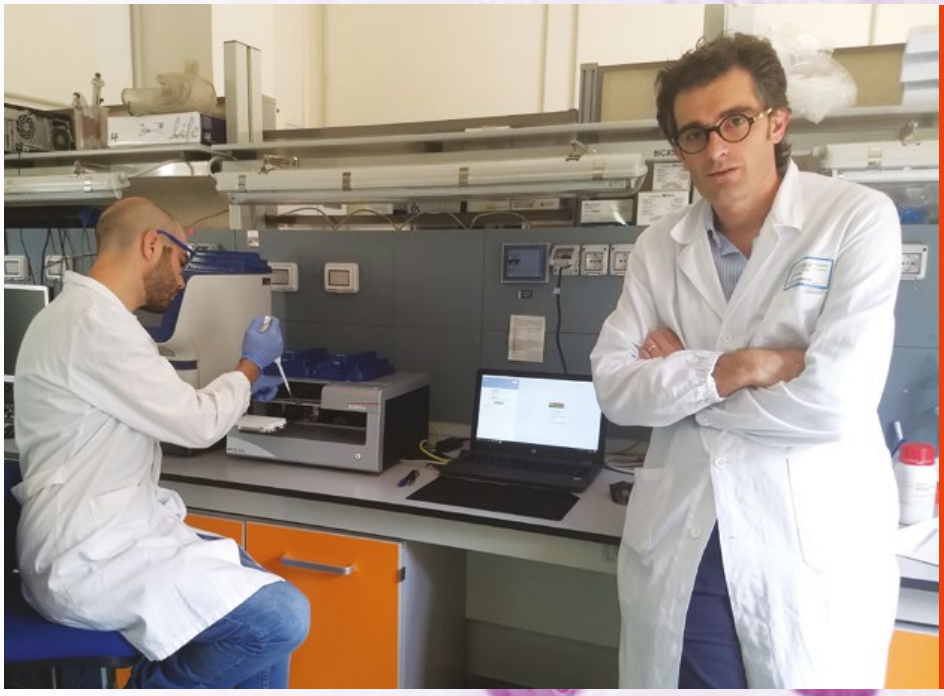
**Developing therapies to treat rare diseases is often hindered by the limited availability of primary patient samples. Without these precious samples, it is difficult to understand the fundamental biology of these conditions or screen compound libraries for drug candidates. A group at the University of Parma is using a 'chemogenomics' approach to overcome this challenge, working on a nanoliter scale to identify new treatments for aggressive pediatric leukemias.**



Acute myeloid leukemia (AML) is an aggressive cancer affecting fewer than 10 in 100,000 people each year in Europe. The resulting scarcity of primary patient samples for *in vitro* testing presents a challenge for drug discovery laboratories seeking out novel compounds to treat them. A recently established group within the University of Parma's Department of Medicine and Surgery aims to address this issue, using a wide range of sample types to investigate various aspects of leukemia and bone marrow transplantation. Physician Scientist Dr Giovanni Roti explained: "After spending several years at the Dana-Farber Cancer Institute in Boston, USA, I returned to Italy last year to set up a new unit for cancer research within the Hematology Unit here at the university. My work in Boston focused on pediatric cancers using chemogenomics – systematic screening of small molecule libraries against individual drug targets or target families – to identify new targets and drugs for aggressive diseases such as leukemia and neuroblastoma, and our work here is a natural progression of that."

The Roti Lab takes a flexible approach to this research, adapting the techniques it uses according to the goal of the study and the samples available. Giovanni continued: "Sometimes we start with a tissue sample, sometimes we use cell lines or cancer models. But the basic process is always the same; start by investigating the cellular biology, then use this understanding to identify and validate therapeutic targets using both biochemical and genetic approaches, including CRISPR/Cas9 knockdown if required. We are currently working on two main projects; one for AML and the other for T-cell lymphoid leukemia (TLL). The AML project started as a chemogenomics screen for a modulator in primary AML, and we are now validating the result of this using the various models available to us in the lab. The second project stems from my previous work in Boston, which identified a modulator of a transcription factor which is frequently mutated in TLL. We are now collaborating with a biotech company to validate a small molecule drug that inhibits this target, with the goal of translating these findings for clinical use."

On starting out, one of the lab's first technology updates was to invest in a Tecan D300e Digital Dispenser, which it now uses in several different applications. "When we screen small molecules, we need to perform titrations to find their $IC_{50}$ values in multiple cell lines or patient samples. Although this is possible to do manually in 96-well plates, it is very time consuming to pipette 12 or 14 different dilutions of up to 10 drugs for each cell type. The D300e simplifies this process considerably, as well as allowing us to work with smaller volumes in 384-well plates without the risk of pipetting errors. It is also really fast, taking between one and four minutes to set up an entire 384-well plate depending on the number of compounds you want to test. We can also perform synergy studies using this technology, which enables us to investigate many dilutions of two or more drugs in combination. This simply wouldn't be possible manually, as the time required for pipetting would compromise the cells."



Andrea Gherli (left) and Giovanni Roti are using the D300e to screen small molecule drugs for AML

> “Essentially, we’re translating our pipeline from bench to bedside in a much shorter timeframe.”

“The speed of the system also offers the exciting prospect of being able to work directly with patient samples to help inform therapies for the clinic. Our goal is to create a system for chemotherapy drugs similar to the antimicrobial sensitivity testing commonly used in clinical environments to guide antibiotic prescriptions. With the D300e, we don’t need a lot of time to set up the early phase of these experiments; we can go from receiving the patient samples to testing compounds in the incubator in just a couple of hours. If we happen to identify a molecule that is already in clinical trials or for another indication, we can ask permission from the local ethics committee to use the drug in patients. In a couple of cases, we’ve actually been able to see a repeat of what we’ve observed *in vitro* in these patients, so it’s proving to be a good prediction of *in vivo* responses. Essentially, we’re translating our pipeline from bench to bedside in a much shorter timeframe.”

“Another feature we really like about the Tecan D300e is that it is very user friendly, and only requires minimal training to set up even complex synergy studies. As a small laboratory, this is a fundamental consideration when investing in any new technology. With only two postdoctoral fellows and two PhD candidates – plus a rotation of students from master’s or undergraduate degrees – I cannot afford to have equipment that is not accessible any time and to everyone. The software automatically calculates how much of each compound is required – and can randomize plate layouts to avoid edge effects – which means that inexperienced users don’t have to perform a lot of calculations to work out the dilutions. Students with limited laboratory experience can therefore use this system without compromising the machine or risking errors, which is a huge advantage,” Giovanni concluded.

**To find out more about Tecan’s drug discovery solutions, visit www.tecan.com/drugdiscovery**

**To learn more about the University of Parma’s Department of Medicine and Surgery, go to** mc.unipr.it

# Cell counting made easy

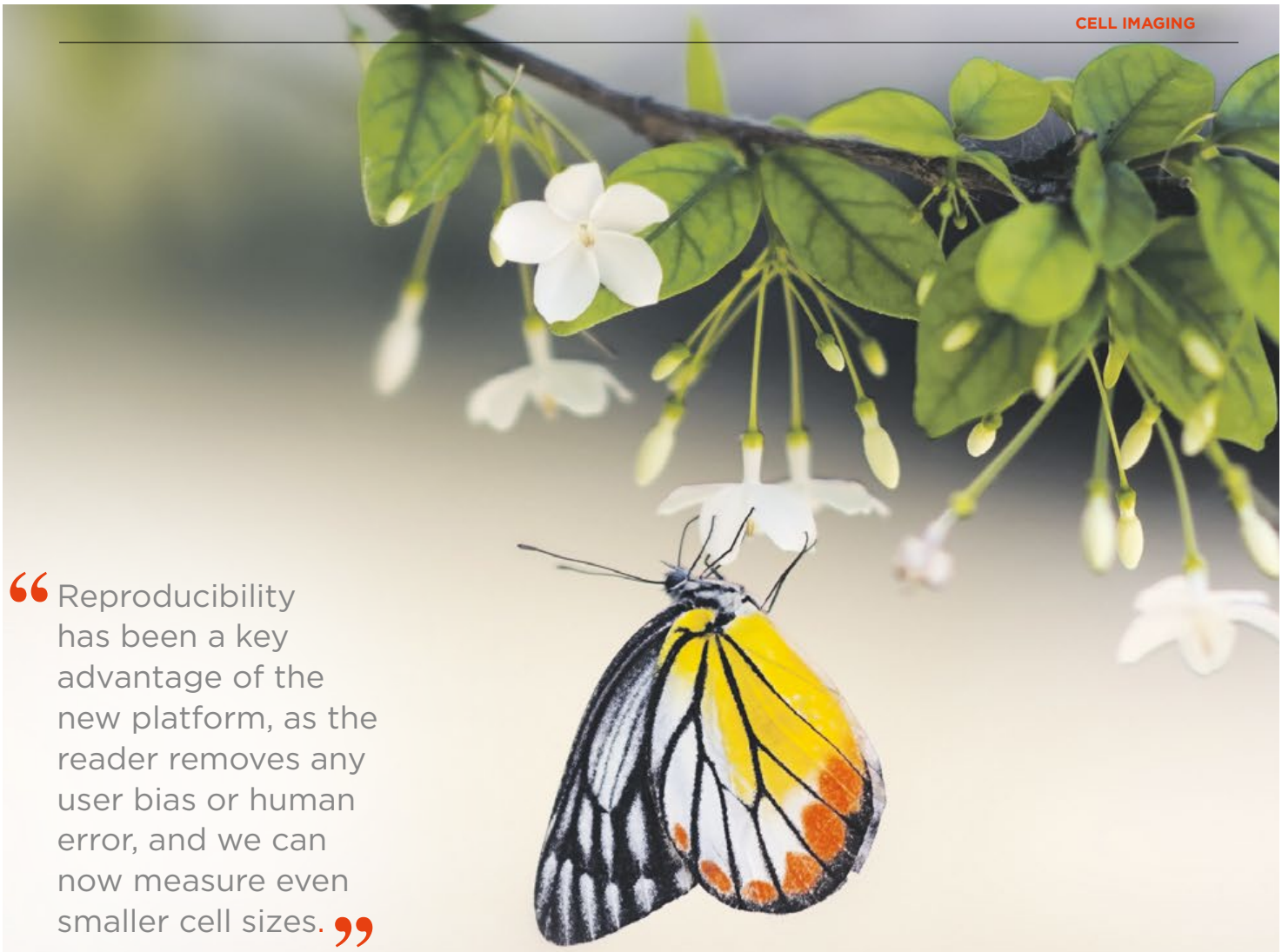
**Small molecule drug discovery involves a range of functional assays that have traditionally relied on manual cell counting techniques to monitor proliferation, migration and invasion. Automated cell counting is enabling the EB House Austria to save time and free up personnel, as well as designing time-course experiments that were previously unachievable.**

The EB House Austria is a unique, highly specialized clinic for patients with epidermolysis bullosa (EB), a rare inherited disease that causes the skin to become 'as fragile as a butterfly's wings', blistering in response to friction or trauma. The clinic, located within the University Hospital of Salzburg, was the initiative of patient organization DEBRA Austria, and opened in 2005. The EB House consists of three units: the EB outpatient clinic; the EB academy; and a research arm developing therapies to treat the disease. The clinic's 30-strong group of researchers is divided across three areas: gene therapy; basic research into cancer and wound healing; and small molecule development and epigenetics. Dr Verena Wally, Group Leader of Small Molecules Research, explained: "The main aim of my group is to identify potential therapeutic targets, while the gene therapy team is hoping to tackle the problem at its root, by replacing or correcting genes using different technologies, such as CRISPR, conventional DNA therapy or trans-splicing."

"Our research covers the full spectrum of the disease, from the milder EB simplex (EBS) to the most severe form – recessive dystrophic epidermolysis bullosa (RDEB) – which ultimately leads to premature death from chronic wounds that develop into cancers. Our initial focus was on EBS, where we discovered an inflammatory pathway that is constitutively activated in the patient population. We repurposed the interleukin-1 beta inhibitor diacerein – which is used in the treatment of osteoarthritis – to treat these patients. This project has since been out-licensed to a pharma company, and has now entered phase III clinical trials. Our attention then turned towards treating RDEB, where we are currently studying differently regulated microRNAs in developing tumors to identify potential biomarkers."

"A large variety of functional assays were needed to support our research, and we purchased a Spark® multimode microplate reader back in 2016 to meet the workload. We carry out confluence measurements for many proliferation, migration and invasion assays, as well as using luminescence to study the interactions of microRNAs with three prime untranslated regions (3'-UTRs), and to assess cell viability with tetrazolium dye MTT assays. We also investigate transfection efficiencies, for example by looking for green fluorescent protein expression."


Members of the EB House research team (left to right): Verena Wally, Michael Ablinger, Thomas Lettner, Roland Zauner, Monika Wimmer and Melanie Böhm



> Reproducibility has been a key advantage of the new platform, as the reader removes any user bias or human error, and we can now measure even smaller cell sizes.

"In September 2017, we purchased the Gas Control Module (GCM™) and Live Viewer, which offered us the expanded functionality we need. The reader has brought huge benefits to our workflow. Previously, we were carrying out migration assays by hand; taking pictures with a microscope and using cell counting software or counting them ourselves. For luminescence assays, we were fortunate to be able to use systems from other departments, but it was time consuming to move between locations, particularly when running time-course experiments.
Reproducibility has been a key advantage of the new platform, as the reader removes any user bias or human error, and we can now measure even smaller cell sizes, expanding the range of cell types we can analyze. In addition, the Spark can handle higher density plates, enabling us to measure a greater number of samples in a single run. We can also now carry out large-scale migration assays involving 12 plates, something we couldn't do previously. Ultimately, the greatest benefits have been the time saved and the personnel it frees up. The platform now runs every day, and is used by all the groups."

"We are currently preparing to run time-course experiments over 24 hours, measuring every two hours to monitor the proliferation and viability among other factors. Before the Spark, we were limited to taking measurements of time points when we were actually in the lab – say after eight hours, 12 hours and 24 hours – but this could lead to us missing the time point that would actually be important. Leaving the plate in the reader and taking readings every two hours will be hugely beneficial. Gone are the days when if we missed the event, we had to start again from the beginning."

"We chose to purchase the Spark on the back of a conversation with another lab, and Tecan's reputation for excellent customer service. We have been impressed by the responsiveness and level of technical support that we have received. We're fortunate to be only 20 kilometers from the Tecan office and, if we have a problem, a Tecan team member gives us a call or visits the site; it was a deciding factor in choosing to upgrade the system," Verena concluded.

**To find out more about live cell imaging, visit**
**lifesciences.tecan.com/live-cell-imaging**

**To learn more about the EB House Austria, go to**
**www.eb-haus.org/en/home.html**

# Empowering CORE oncology research

**Christophe Deben and the team at the University of Antwerp's Center for Oncological Research (CORE) were the lucky recipients of a fully loaded Tecan Spark® Cyto plate reader with live cell imaging and real-time cytometry, after winning a Tecan competition in October 2019. The center is now using the instrument to support its revolutionary research in immuno-oncology.**

Center for Oncological Research (CORE) University of Antwerp

The Spark Cyto competition, which ran from April to September 2019, required labs to submit a written proposal explaining how they would use this unique plate reader's live cell imaging and real-time cytometry capabilities to further their research and advance scientific understanding. A panel of expert judges selected a shortlist from over 100 entries, and each finalist was invited to give a short webinar presentation providing further details of their research plan. The winner was Dr Christophe Deben, a postdoctoral researcher at the University of Antwerp, who explained his work: "Our lab is primarily focused on translational research and combination therapies for non-small-cell lung cancers and pancreatic cancers. At present, my own work is on the use of patient-derived organoids in *in vitro* studies to characterize oncogenic signatures and explore novel therapies."

"When you use commercially-available cancer cell lines for experiments, you can see if a certain therapy has an effect or not, but the downside is that these cell lines have been in culture for a very long time. This means that the cells acquire characteristics that may no longer be relevant to a patient's tumor. Instead, we work closely with Antwerp University Hospital, using material from tumor biopsies to generate both 2D and 3D spheroid models, allowing us to study how individual cancers respond to therapy."

"The culture conditions for each tumor type need to be optimized to grow in the lab as an organoid, so any technology that makes these studies more streamlined and efficient is a huge advantage. Previously, we relied on standard flow cytometry or basic microplate-based assays for these

Christophe Deben and the team at the University of Antwerp's Center for Oncological Research



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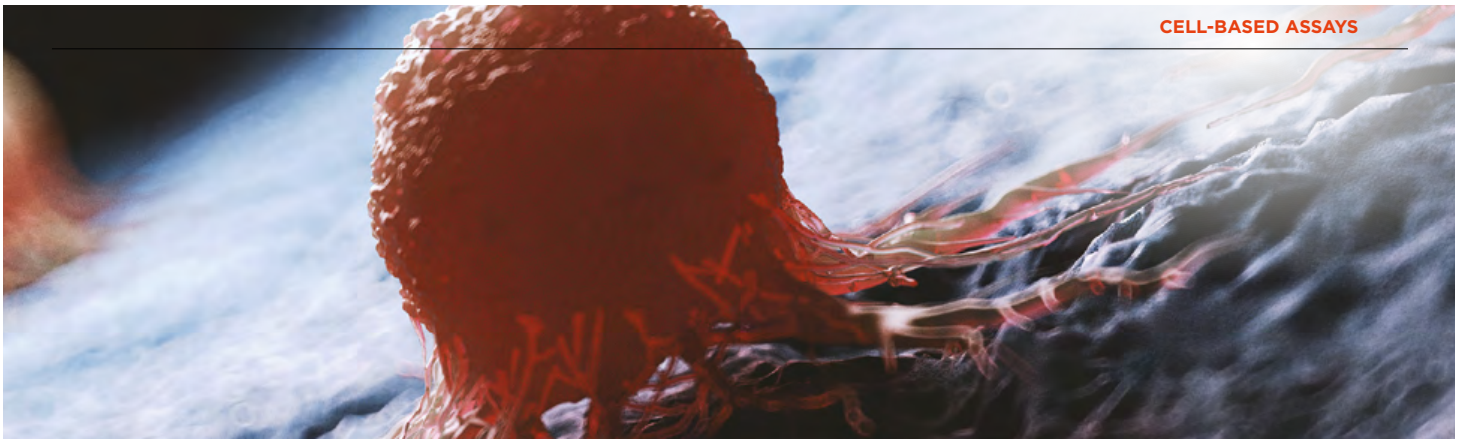


experiments, but the drawback of those techniques is that you need a lot of cells to form a large enough number of organoids to study. This is very expensive, and can be difficult to achieve with limited patient material. My goal was to miniaturize all the assays, but still get enough data; I wanted to do everything in 384-well plates, reducing the number of cells required, as well as the amount of media and reagents. This was why I entered the competition to win the Spark Cyto, and it's opened up a world of possibilities!"

"Using the Spark Cyto for this work is fantastic, giving us much deeper insight compared to standard singleplex methods. I let my imagination run wild in creating the experimental set-up for the competition, and it amazes me that nearly everything I thought of is possible with the Spark Cyto!"

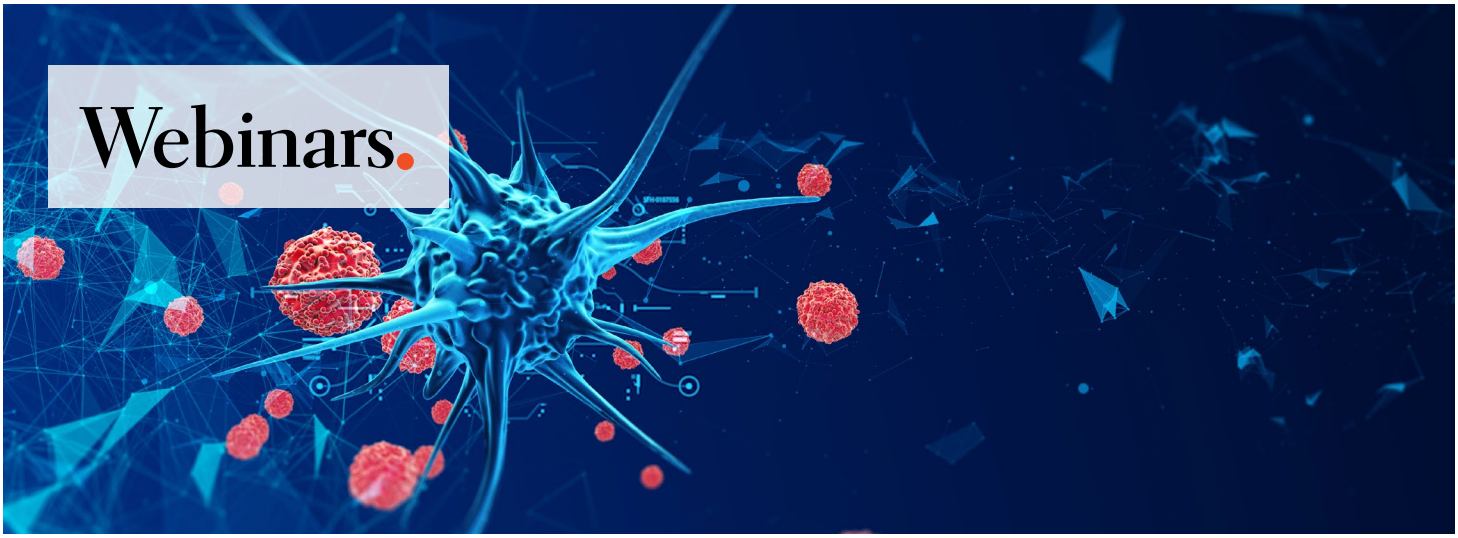
The Spark Cyto is proving the perfect partner for CORE's research, combining the features of multiple analytical instruments into one system. Christophe continued: "We already had an older live cell imaging instrument, but it's not really made for spheroid work. Plus, with the Spark Cyto, you can multiplex live cell imaging with just about anything. I can now combine it with different fluorescent markers, as well as assays based on luminescence. Using the Spark Cyto, I can get so much more information about how the cells are responding to certain therapies, offering more clinical understanding and allowing better translation of *in vitro* results into the likely responses that can be expected in patients. I really can do everything that I want to do with just one experiment now – instead of having to visit several labs to use various instruments – and I can monitor everything in real time, it's fantastic. Most of our experiments are now automated, so I can spend more of my time analyzing data or further optimizing our assays, rather than physically running the experiment. With a couple of hours' work in the lab, I can prepare the samples and load them into the Spark Cyto, then simply let it run – generating a week's worth of data for analysis."

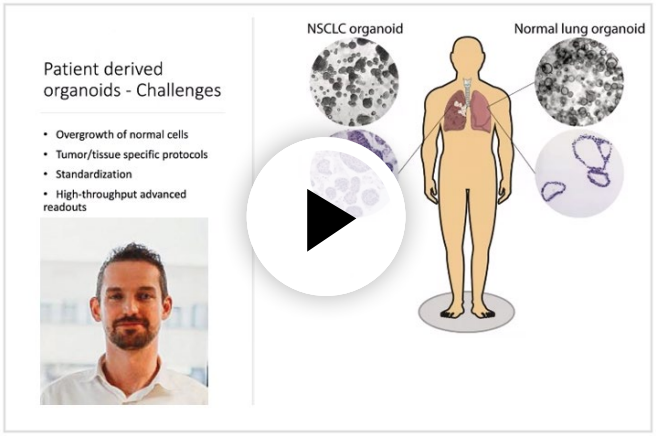
"We have also recently purchased a D300e Digital Dispenser from Tecan, which allows us to 'print' drugs of interest in very small volumes directly into a microplate. This instrument can be used with the Spark Cyto to give us even more experimental data, by allowing us to test different drug combination strategies and therapies in much less time. For example, I studied two or three drug combinations during my PhD, but it was a lot of work and was incredibly time consuming, taking a full year to perform all the assays. Now, I could do the same experiments in a month – this set-up is an amazing time saver, and has really increased both the speed and reproducibility of our research. In a clinical setting, doctors want to test patient samples with up to 18 different clinically-approved compounds at a time, which would now not be a problem with the Spark Cyto and D300e. We are not limited to certain combinations or drugs, and can quickly see which combinations work best *in vitro* – it opens the doors for personalized medicine."

"We are extremely grateful to Tecan for picking our lab as the winner of this competition, and our interactions with the company – particular the application specialists – have been very good. We've learnt a lot from each other, making adjustments to the protocol and software to work optimally with our 3D spheroids. For now, our work is purely research, but our long-term goal is to move into a clinical setting. Using the Spark Cyto for this work is fantastic, giving us much deeper insight compared to standard singleplex methods. I let my imagination run wild in creating the experimental set-up for the competition, and it amazes me that nearly everything I thought of is possible with the Spark Cyto! The versatility of the instrument means that we can use it for nearly every line of research running at CORE, and we look forward to where it will take us," Christophe concluded.

**To find out more about Tecan's Spark Cyto, visit**
**www.tecan.com/sparkcyto**

**To learn more about the Center for Oncological Research, go to**
**www.uantwerpen.be/en/research-groups/core/**




**Semi-automated multiplex assays for monitoring therapy response in patient-derived 3D organoids**

This webinar explains how you can set up experimental workflows and multiplex analysis techniques to monitor drug responses in real time. Patient-derived organoids are treated with drugs using the D300e Digital Dispenser and analyzed with fluorescence imaging and luminescence-based viability assays using Spark® Cyto.

**Dr Christoph Deben**
Postdoctoral researcher
Center for Oncological Research
University of Antwerp

WATCH WEBINAR


**New methods to better predict patient drug responses in cancer organoids using a multimode imaging plate reader**

Pancreatic cancer is a deadly malignancy with few treatment options. This webinar highlights how dynamic measurements of confluence in patient-derived organoid models of pancreatic disease can predict treatment responses.

**Asst. Prof. Dannielle Engle**
Assistant Professor
Regulatory Biology Laboratory
Salk Institute for Biological Studies

WATCH WEBINAR

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# Featured products.

**D300e Digital Dispenser** dispenses picoliter volumes of drugs in stock concentration directly into assay plates to create dose-response curves. The D300e supports plate formats of up to 1,536 wells and is therefore ideal for miniaturization at low to medium throughput.

- Reagent dispenser for small volumes (11 pl – 10 ul)
- Application: dose response curves, drug-drug combinations
- Solvents: DMSO & water based
- Molecules: small chemical, antibodies, proteins, nucleic acids

For Research Use Only. Not for use in diagnostic procedures.
Tecan D300e Digital Dispenser is a product of HP Inc. CA, USA.

LEARN MORE

**Spark® multimode reader** combines conventional read modes with incubation features and bright field imaging in a modular setup. A stacker can be attached to automate reading of up to 50 plates.


- Combine over 20 modules
- Absorbance, fluorescence, TRF, TR-FRET, FP, luminescence, imaging, Alpha technology
- Incubation options for working with cells
- Upgradable
- Stacker option for up to 50 plates

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LEARN MORE

**Spark Cyto multimode reader** with live cell imaging combines Spark multimode reader with automatic fluorescence imaging capabilities. Microplates can be analyzed with conventional read modes and fluorescence imaging in separate or combined scripts.


- 4 configurations
- Plate imaging (bright field and fluorescence – 4 colors, 3 magnifications)
- Absorbance, fluorescence, TRF, TR-FRET, FP, luminescence, Alpha technology
- Incubation options for working with cells
- Stacker option for up to 50 plates

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**Tecan – Who we are.**

Tecan is a leading global provider of life science laboratory instruments for biopharmaceutical, forensic, clinical diagnostic and academic markets, specializing in the development and production of automation and detection solutions, including imaging and microplate readers, microarray products and washers.

Founded in Switzerland in 1980, Tecan has manufacturing and R&D sites in both North America and Europe, and maintains a sales and service network in 52 countries. To date, Tecan has distributed approximately 20,000 microplate readers worldwide, and is committed to continuous technological improvements and compliance with the highest global quality standards.

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