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WELCOME TO THE THIRD SCIEX VISION

The mass spectrometry field is currently enjoying strong growth, thanks to the unique information and insights this technology can provide. MS is inspiring new approaches to problems old and new, opening up exciting new areas in fields well outside the traditional LC-MS market. This issue of SCIEX VISION showcases the breadth and depth of the MS space, from forensics and toxicology to drug development and biomarker analysis.

The use of mass spectrometry in the 'omics' disciplines – particularly proteomics, metabolomics and lipidomics – has seen rapid progress in the last few years. You'll find several articles discussing the diverse ways in which SCIEX MS instruments (and capillary electrophoresis systems) are being used around the world to further our understanding of fundamental biology, and how that may translate to a new understanding of disease.

The advent of robust and easy-to-use MS instruments designed for routine testing – such as our X-series QTOF Systems – has also improved accessibility to these powerful technologies. Environmental testing, where large sample numbers are commonplace, is one area benefitting from this approach, as demonstrated by the work being undertaken at the IDEA-CSIC (pages 4-5). Coupled with continued growth in traditional markets, such as drug discovery and development, the future is bright for the MS sector. Here at SCIEX, we're in a privileged position, playing a central role in many of our customers' workflows – from instruments and software to services – to help them address their most pressing scientific questions.

I hope you enjoy this issue.

Joseph Fox

Senior Vice President of Global Sales and Service, SCIEX

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TAKING CARE OF THE ENVIRONMENT

Damià Barceló, Research Professor at the IDAEA-CSIC and Director of the Catalan Institute for Water Research

Spanish scientists engaged in environmental analysis are taking advantage of high resolution mass spectrometry to investigate emerging contaminants in water, exploring the fate, distribution and elimination of compounds such as pesticides and pharmaceuticals. The data obtained is then used to provide an indication of the potential risk to biota and the environment in general, with a view to enabling regulatory bodies to update legislation.

Emerging contaminants in water, such as pesticides and pharmaceuticals, pose a potential risk to both plant and animal life. This crucial area of environmental research is the focus of the Water and Soil Quality Research Group at the Department of Environmental Chemistry, Institute of Environmental Assessment and Water Research (IDAEA), Spanish National Research Council (CSIC), in Barcelona. Damià Barceló, Research Professor at the IDAEA-CSIC and Director of the Catalan Institute for Water Research (ICRA) in nearby Girona, explained: "Our main area of interest is the study of contaminants in water and their environmental impact on, for example, fish and other organisms in rivers. This includes both substances that have been around for many years, such as the pesticides 2,4-D and 2,4,5-T, and those that are new to the market."

Damià continued: "Our multidisciplinary teams – including engineers, aquatic specialists, microbiologists and chemists – perform what is known as advanced monitoring, looking for emerging contaminants that are not included in the current legislation. We take a stakeholder approach to these studies, involving representatives from the various regulatory bodies and water authorities that will ultimately rely on the results to update guidelines and legislation. Essentially, we identify and quantify the contaminant using mass spectrometry, do a risk assessment of its likely environmental impact, and communicate this to all the interested parties so that they have a complete understanding of the situation. Armed with this knowledge, they can decide whether or not the chemical needs to be added to the existing legislative database."

"Around 80 percent of our work is focused on continental waters – water from rivers and lakes – although we also do some marine studies. Typically, we analyze water from Spanish rivers, such as the river Ebro, which we collect ourselves, and are also involved in European collaborations studying the Sava – which runs through Slovenia, Croatia, along the Bosnia-Herzegovina border and into Serbia – the Adige in Italy and the Evrotas in Greece. In these cases, samples are shipped to us from our colleagues in other countries. In addition, we carry out some exposure

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experiments in the lab, investigating the ecotoxicity of, for example, nanomaterials and microplastics, to establish the potential environmental risk they present."

"The first stage of any analysis is sample preparation. If we are looking at solid samples – fish or soil sediment, for example – this entails homogenization followed by pressurized liquid extraction. Water samples are generally prepared for MS analysis using solid phase extraction, which can be performed on- or offline. The degree of clean-up required depends on the water source, with wastewater needing more extensive purification than drinking water. MS sensitivity has improved tremendously over the years; today's instruments are sensitive enough to detect contaminants at levels as low as nanograms per liter, which means that we only need to analyze five or 10 milliliters of a sample compared to as much as a liter a couple of decades ago."

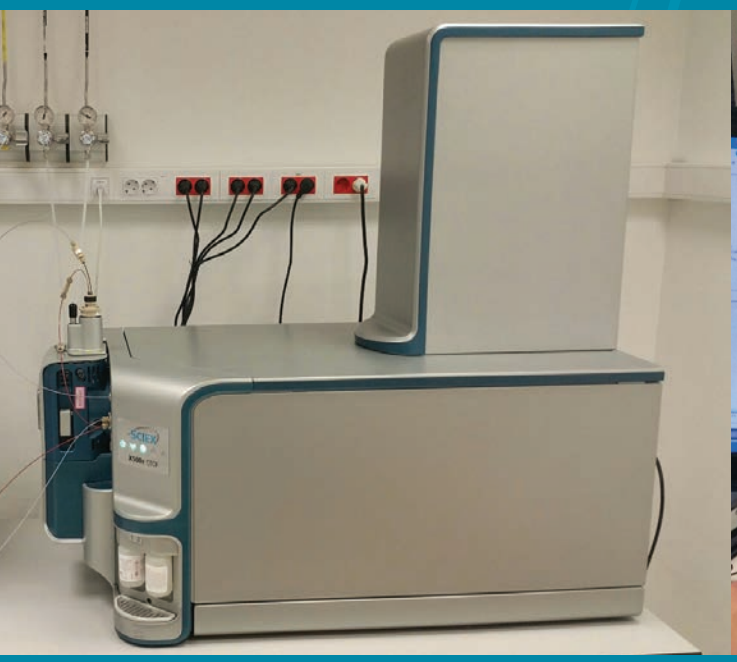
"We have a number of SCIEX instruments in our labs, including Triple Quads and QTRAPs, and our most recent acquisition, the X500R QTOF System. The big advantage of the X500R is that, as a high resolution instrument, it allows us to perform accurate mass measurements. This is a real asset for the type of work we are doing, where we need to identify a host of unknown compounds and metabolites. Another major benefit of this instrument is SWATH Acquisition, a data independent acquisition technique that is a very powerful tool for non-targeted analysis of new chemicals. We've had the X500R for about 18 months now, and were able to adapt our existing methodologies for use with this system relatively quickly as we were already familiar with SCIEX software. These methods will be further developed as necessary to incorporate additional chemicals. Our target is to analyze as many compounds as possible in the same run, aiming for between 75 and 100 per analysis."

"At the moment, the X500R is mainly used for qualitative and quantitative analysis of pharmaceuticals in wastewater destined for reuse in agriculture – which is a hot topic in Europe – and it is performing well. We are very happy with it and will be exploring its capabilities further still in other studies. MS technology has come a long way in recent years, and the X500R is a competitive instrument in the marketplace. In my view, this new generation of QTOF makes life in the lab better," Damià concluded.

> "[THE X500R] IS A REAL ASSET FOR THE TYPE OF WORK WE ARE DOING, WHERE WE NEED TO IDENTIFY A HOST OF UNKNOWN COMPOUNDS AND METABOLITES."

To find out more about the Institute of Environmental Assessment and Water Research, visit **www.idaea.csic.es**

To find out more about the SCIEX X500R, visit **www.sciex.com/x500r**



EXPLORING THE FOOD METABOLOME

Translational nutrition explores the changes that occur throughout plant development, harvesting, storage, transport and consumption, and the impact that these changes have on human or animal health. Dr. Colin Kay, Associate Professor of Translational Nutrition at the Plants for Human Health Institute in North Carolina, is exploring an exciting new area, studying the phytochemicals found in different foods to link these compounds to microbial biosignatures and the food metabolome.

Dr. Colin Kay, Associate Professor of Translational Nutrition at the Plants for Human Health Institute

It is becoming clearer that the vast majority of phytochemical metabolites found in the human circulatory system are associated with transformations caused by microbes in the intestine. Larger phytochemicals are often broken down into 30 or more smaller metabolites and, as most food sources contain dozens to hundreds of phytochemicals, the number of metabolites can be extensive. Dr. Colin Kay works in the field of translational nutrition, which aims to better understand these metabolic transformations and their impact on health and disease, as he explained: "After completing my PhD in nutritional biochemistry, my career has mostly focused on dietary small molecule metabolites. My work now is establishing microbial biosignatures of the food metabolome by analytically exploring metabolites in human and animal samples. We're mainly studying cardiovascular disease, diabetes, metabolic syndrome and aging, trying to identify how food biosignatures correlate with disease risk. If you can identify areas of the biosignature that are associated with specific improvements or deteriorations, then you can say that eating more or less of a certain food will impact the development of a particular disease over time."

Colin continued: "A lot of our work – about 80 % – is analyzing clinical samples from other groups by MS/MS, but we also run our own clinical studies, and this means that our MS platforms are running 24/7. We're currently developing targeted MS methodologies to search for 100 to 150 compounds in a single run. This will allow us to identify differences between either treatment and placebo, or different dietary sources, to find biosignatures that are unique to, or predictive of, either a food or a disease endpoint. We began by studying the blueberry, because that was the food we had the most data for. Since then, we've spent around two years collecting data on other polyphenol-rich foods, and I predict it'll take another three to five years just to finish this area. Our overall goal is to develop a complete food metabolome database, which can then expand by need, focusing on certain food groups based on high consumption or confounders seen in our dietary interventions. The hope is that the more data we generate the more metabolite overlap we'll see between different food profiles."

"Every human has a different microbial profile (or microbiome), and so there is extensive variability between samples. This means we need high precision and accuracy to establish useful biosignatures. Some compounds, such as hippuric or uric acid, are common metabolites of most foods or basic metabolic processes, and the range for these analytes can vary significantly – between about 10 nM up to 100 µM. We've therefore had to optimize our methods to create windows and thresholds that are robust enough to capture both

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> "THE ABILITY TO OPTIMIZE AND ALTER ALL OF THESE PARAMETERS IN OUR METHODOLOGY TO SUCH A HIGH EXTENT USING THE SCIEX SYSTEMS HAS BEEN EXTREMELY USEFUL."

high and low concentration analytes to characterize changes above background levels; we have had to use 12- to 14-point standard curves to establish linearity in some cases. We're also constantly looking for new analytes, and it can be hard to prove that some of these metabolites are real without access to suitable reference standards. With many MS systems, it isn't possible to adjust numerous compound-dependent fragmentation parameters – for example, voltages and collision gases – to allow accurate identification of a genuine precursor compound over a gas-phase artifact or a product of in-source fragmentation. In contrast, the SCIEX QTRAP 6500+ that we currently conduct most of our work on is excellent for characterizing unknown compounds; it has a large number of parameters that can be altered relative to compound and source optimization – it's incredibly versatile. Our workflow goes from optimization in MRM to scheduled MRM, and finally to advanced scheduled MRM. The advanced scheduled MRM algorithm enables us to optimize peak windows, thresholds and dwell weights for every analyte transition, allowing for peak optimization in complex mixtures without significant loss of cycle time."

"The SCIEX QTRAPs are at the center of a lab like ours, where workflows are continuously developed and enhanced. Due to their versatility and high cycle time, they are ideal for method development and validation, as well as running high throughput methods. We need to make the most of our instrument runtime, which is around 87 to 90 hours for a 96-well plate. Being able to change parameters – such as dwell time – ensures that we can maximize the sensitivity for even low-level analytes. The ability to optimize and alter all of these parameters in our methodology to such a high extent using the SCIEX systems has been extremely useful. I've used SCIEX instruments for about 12 years now. When I was working in the UK, we tested a sample of mixed metabolites on MS platforms from different manufacturers, and SCIEX was the one that really shone – I've stuck with them ever since," Colin concluded.

To find out more about the work of Colin Kay, visit **plantsforhumanhealth.ncsu.edu/people/colin-kay/**

To find out more about the SCIEX QTRAP® 6500+ System, visit **www.sciex.com/qtrap-6500plus-system**

A ONE-STOP SYSTEM FOR ACADEMIC RESEARCH

The breadth of research in a university academic lab requires a mass spectrometer that offers the sensitivity and resolution to accommodate multiple applications and samples. The platform also needs to be robust and suitable for use by students with differing levels of experience, while delivering reproducible, reliable results. Choosing a single instrument to meet these criteria is an important decision, and the College of Pharmacy at Chungnam National University considered its options very carefully before choosing SCIEX.

The College of Pharmacy at Chungnam National University in Daejeon, South Korea, provides both teaching and practical training to undergraduate and graduate students, alongside research in fields such as pharmacotherapy and drug discovery. Associate Professor Young G. Shin, an academic and researcher at the college with a special interest in drug metabolism and pharmacokinetics (DMPK), explained: "I began my career at Seoul National University up to my PhD, and then moved to the USA to take up a postdoctoral position at the University of Illinois. Here, I used a single quadrupole mass spectrometer to screen for small, drug-like compounds in natural products with anti-cancer or cancer chemoprevention effects. Although I had some mass spectrometry experience, particularly in GC-MS, this was the first time I had used electrospray; I'd never seen it before and, for that time, it was amazing."

Associate Professor Young Shin from the College of Pharmacy at Chungnam National University

Young continued: "Later, I moved to the east coast, working in the DMPK group of a global pharma company. In such a large company, with people working on all aspects of drug discovery and development, I was able to really build up a tremendous amount of knowledge. This held me in good stead when I had the opportunity to join a biotech company in California, studying not only small molecules but also monoclonal antibodies, or biologics. Some years later, I returned to Chungnam National University, and was glad to be able to share my practical knowledge of the industry with the students, complementing the academic curriculum. I could also continue to follow my research interests – quantitation of small molecules, peptides, oligonucleotides, therapeutic antibodies and antibody-drug conjugates (ADCs); metabolite identification for small molecules and peptides in plasma, urine, bile or feces; and deconvolution of monoclonal antibodies and drug-to-antibody ratio analysis for ADCs in plasma or serum – as well as collaborating on DMPK projects with pharmaceutical and biotech companies in South Korea."

"When I made the transition back to academia, I needed to buy a mass spectrometer. However, funding was limited, and so I asked my former colleagues in the US 'If you could only buy one instrument for all your research projects, which one would you choose?'. I explained that I needed high resolution to support metabolite identification, as well as high sensitivity for small molecule and peptide analysis, and pharmacokinetic (PK) studies, and they recommended

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the SCIEX TripleTOF 5600 System. The various types of mass spectrometer – triple quadrupole, ion trap, time of flight (TOF) – have different benefits, but the TripleTOF 5600 offers the best overall combination of high resolution and sensitivity for my work, and allows me to investigate everything I want to on a single instrument."

"For a standard PK study, we frequently work with up to 150 samples per study, with a throughput of around 400 to 500 samples a week, quantifying small and large molecules in biological samples using high resolution selected reaction monitoring. I've been very impressed by the instrument's sensitivity and reproducibility. Typically, we're looking at a lower limit of quantification of around 1 ng/ml for PK studies, and we consistently achieve this with the TripleTOF 5600; if greater sensitivity is needed, we have access to a SCIEX Triple Quad 6500 in our core research center on campus. The TripleTOF is also heavily used for metabolite identification, allowing us to determine the origin of a particular fragment or daughter ion. We begin with a TOF full scan to look for unique metabolites and any related peaks, followed by a product ion scan. The good thing about a TOF full scan is that all the information is captured in a single run, so it's a good starting point for identifying any metabolites or unknown compounds in a sample."

> "THE TRIPLETOF 5600 OFFERS THE BEST OVERALL COMBINATION OF HIGH RESOLUTION AND SENSITIVITY FOR MY WORK, AND ALLOWS ME TO INVESTIGATE EVERYTHING I WANT TO ON A SINGLE INSTRUMENT."

"The TripleTOF 5600 has become the workhorse of my lab, and its robustness is critical to our collaborative work with pharmaceutical and biotech companies. Our partners are obviously interested in the commercial aspects of the research, and there is a demand for high quality results with a short turnaround time. Consequently, I can't afford downtime extending beyond two days and need an instrument that requires minimal ongoing maintenance. In an academic lab, where many students are using the same instrument, maintenance can be an issue. This was one of my biggest considerations when investing in a mass spectrometer, but it hasn't been a problem. The TripleTOF 5600 is ideal for a training environment; I have more than 10 students using the instrument on a daily basis and haven't had any serious problems. If I have any minor concerns with the system, I know I can immediately turn to SCIEX for technical support and will receive excellent service within 48 hours, which is amazing. In light of all of these factors, choosing the TripleTOF 5600 has been a good decision. I've been using the instrument for over five years now – generating more than 100 reports for submission to regulatory agencies – and its high quality, speed and robustness have made it perfect for my work," Young concluded.

To find out more about the College of Pharmacy at Chungnam National University, visit **plus.cnu.ac.kr/html/en**

To find out more about the SCIEX TripleTOF® 5600+, visit **www.sciex.com/tripletof-5600**

CESI-MS – THE DRIVING FORCE BEHIND VOLUME-RESTRICTED METABOLOMICS STUDIES

Metabolomics studies often encounter difficulties due to the limited sample volume available for analysis. Researchers at the Leiden Academic Center for Drug Research in the Netherlands are using capillary electrophoresis-mass spectrometry to overcome this challenge by developing microscale analytical workflows for volume-restricted metabolomics.

The Leiden Academic Center for Drug Research (LACDR) is a multidisciplinary center of excellence for drug discovery and development. The use of 3D microfluidic organ-on-a-chip systems employing patient-derived induced pluripotent stem cells, primary cells and mouse models of disease for (translational) research studies inevitably limits the amount of biological material available for analysis. To overcome this issue, LACDR's Biomedical Microscale Analytics group is developing microscale analytical tools and workflows for metabolic profiling of volume-limited biological samples, as Principal Investigator Rawi Ramautar explained: "During my PhD, I became more and more fascinated by the important role of separation sciences in obtaining a better understanding of the pathological mechanisms of diseases. Therefore, I decided to follow a career in the development of analytical techniques in metabolomics, as this approach is highly suited to gaining insight into disease biochemistry."

Rawi continued: "There was one particular technology that I thought would fit my ambition – capillary electrophoresis-mass spectrometry (CESI-MS). Capillary electrophoresis is easily integrated with electrospray ionization mass spectrometry, and is well suited to in-depth profiling of highly polar and charged metabolites in size-limited biological samples. A significant fraction of the metabolome is composed of polar and charged metabolites, and so CE can be considered a very strong separation technique for this purpose as compounds of interest are separated on the basis of their (intrinsic) electrophoretic mobilities. CE also has the advantage that nanoliter volumes can be injected from just a few microliters of sample, achieving nanomolar detection limits. By selectively concentrating acidic or basic metabolites within the capillary, it is even possible to reach sub-nanomolar detection limits. This makes CESI-MS a very strong tool for trace level analysis in volume-limited samples, although at that time it had hardly been explored for metabolomics."

Rawi Ramautar, Principal Investigator at the Leiden Academic Centre for Drug Research

"As we have gained experience in the use of CESI-MS we have published our protocols so that other researchers can benefit from this approach to metabolomics. We have seen a great deal of interest in the technique, as people are often reluctant to develop such tools themselves because of a lack of experience in electro-driven separation techniques. They frequently ask to visit our lab to see how we approach the work, as well as asking if we can help with training. It's a good sign when scientists from both academia and biotech companies are showing an interest in our CESI-MS protocols for metabolomics studies."

"Longer term, we recently invested in a SCIEX TripleTOF 6600 System, and our ambition is to be the first group in the world to assess the use of CESI in combination with SWATH MS, as we believe this will alleviate the bottleneck of metabolite identification. In addition to volume-limited metabolomics, we plan to explore the use of CESI-MS for chiral metabolic profiling, focusing on D- rather than L-metabolomes, and also for the analysis of (neuro)peptides, peptides containing D-amino acids, and for nanoparticle-based metabolomics studies."

"Collaborative studies are an important part of advancing CESI-MS, and we have been working with SCIEX for a long time now," said Rawi. "It's good for academic partners to get involved in the further development of new techniques, and I think we are one of the most important collaborators in the metabolomics sector. SCIEX takes our input seriously, using it to make its products better and better. This is to our advantage, because the better the product is, the better the science we can do. It's a great partnership."

"The development of the nanoVials – allowing multiple injections to be performed from just a few microliters of a precious sample – perfectly illustrates how SCIEX responds to feedback from the scientific community. The nanoVials enable, for example, replicate analysis in both positive and negative ion modes, or evaluation of peptides instead of metabolites. This provides maximum biochemical information from a single, often scarce, sample – something the community had long desired. But the software is just as important as the hardware. The most recent SCIEX OS software is particularly user friendly, making it ideal for day-to-day operation and training, and I think it will get easier still as it is developed further. I also have very good experiences of PeakView, which can be used in a straightforward way to evaluate your data."

Sharing information, whether through collaborative studies, publications or conferences is essential for the continued development of CESI. "It's important to understand the science behind each step that you are taking, why something is done in a particular way, and to share experiences with other researchers, biotech companies and manufacturers. SCIEX is leading the way with an annual Global CESI-MS Symposium that is open to the whole community. This gives us a chance to learn from our peers, and to discuss our collaboration and provide feedback to SCIEX. More and more people are attending the symposium each year, which is a good sign for the future of CESI-MS," Rawi concluded.

> "CAPILLARY ELECTROPHORESIS IS EASILY INTEGRATED WITH ELECTROSPRAY IONIZATION MASS SPECTROMETRY, AND IS WELL SUITED TO IN-DEPTH PROFILING OF HIGHLY POLAR AND CHARGED METABOLITES IN SIZE-LIMITED BIOLOGICAL SAMPLES."

To find out more about the Biomedical Microscale Analytics group, visit **www.universiteitleiden.nl/en/science/drug-research/systems-pharmacology/biomedical-microscale-analytics**

To find out more about the SCIEX CESI 8000 Plus ESI-MS system, visit **www.sciex.com/cesi8000**

UNDERSTANDING THE METABOLOME

Cellular metabolism is a complex, interconnected network of chemical reactions that are vital to ensure cell growth and survival. Thousands of chemical pathways operate in parallel to control every process from metabolite absorption to lipid, protein and energy production. Prof. Dr. Markus Ralser, Group Leader of the Molecular Biology and Metabolism Laboratory at the Francis Crick Institute and Einstein Professor in Biochemistry at the Charité – Universitätsmedizin Berlin, is conducting one of the largest proteome projects to date, connecting every gene in yeast to its role in enzyme expression and metabolism.

Prof. Dr. Markus Ralser, Group Leader of the Molecular Biology and Metabolism Laboratory at the Francis Crick Institute and Einstein Professor in Biochemistry at the Charité – Universitätsmedizin

A deeper understanding of the metabolome – which has links to ageing and major diseases, such as cancer and neurodegenerative disorders – has significant implications for the development of therapies for multiple conditions. Indeed, the metabolic network is a dynamic matrix of hundreds or thousands of chemical reactions occurring in parallel. Fluctuations in the cellular environment cause multiple reaction changes, yet how the cell recognizes which reactions to change and when to respond is poorly understood. This lack of understanding makes identifying metabolic targets required for drug development challenging, and often leads to using laborious and costly trial-and-error investigations. Markus realized his interest in metabolism after completing a PhD studying proteins linked to spinocerebellar ataxia. He explained: "When I started to look at metabolism, I saw that, although metabolic problems are very complex, you can address them efficiently. It is relatively straightforward to design experiments that are going to answer your investigational questions, compared to many other biological disciplines, and this excited me. I originally set up my own lab studying metabolism at the Max Planck Institute for Molecular Genetics in Berlin. From there, I moved the lab to Cambridge, and I'm now based in the Francis Crick Institute in London and at the Charité in Berlin."

"We're trying to understand how the cellular metabolic structure is constantly maintained, which genes control metabolism, and how these genes are linked. We're studying yeasts because they have a eukaryotic cell structure; they combine the complexity of the metabolism of a higher organism with the simplicity of handling a microorganism, which is why it is important to design new yeast strains for use in biotechnology applications. There are also a lot of tools available for working with yeasts, and they grow easily. We have created a genetic library of about 5,000 gene deletion strains, allowing us to model each

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gene and its role in metabolism. Changes in metabolite levels for each strain have already been recorded, and we are now connecting each strain's proteome. We are using three TripleTOF 6600 Systems from SCIEX for this project because of their sensitivity and accuracy, and their ability to perform data independent SWATH Acquisition in fast gradients. Unusually for a proteomics project, we run two of the TripleTOFs with capillary flow LC, and one with high flow LC. This allows us to achieve a fast chromatographic runtime while maintaining robustness and chromatographic quality, as required in SWATH MS. We also have a fully automated sample preparation workflow, which helps increase productivity, and we have even programmed software to take the raw data from the SCIEX systems and deconvolute the SWATH spectra, specifically to improve the analysis of fast proteomic methods."

"I think this collaborative study between SCIEX, the Cambridge Centre for Proteomics at the University of Cambridge, and ourselves at the Crick is perhaps the most systematic large proteome project currently running globally, and our aim is to expand it further by recording (single-cell) transcriptomes and lipidomes. We can then connect this information to changes in enzyme levels, and we hope to be able to explain specific phenotypes. This will give us a good overview of yeast metabolism, which we can use as a template for understanding human metabolism. Five or six years ago, the classic proteomics workflows simply couldn't handle looking at such large data sets, and the technology wasn't as precise – you could easily end up measuring noise, or you could inject the same sample three times and see three different peptides. The SCIEX TripleTOFs have transformed the way we can analyze samples, as they offer very high precision and reproducibility, which is so important when trying to quantify 5,000 gene-metabolism interactions."

"We have had really positive communications with the SCIEX team, and they are interested in how we altered the SWATH workflow, and how we calculate false discovery rates. With their expertise, we hope we can improve the software further. We're actually in the process of publishing our software, and hope that other people will be able to use it to further their own research. There are a lot of ideas out there from different groups, and so I'm positive that in the future there will be more modifications of the SWATH protocols to create a library of hybrid versions, helping to move research on faster – it's an exciting prospect," Markus concluded.

> "THE SCIEX TRIPLETOFS HAVE TRANSFORMED THE WAY WE CAN ANALYZE SAMPLES, AS THEY OFFER VERY HIGH PRECISION AND REPRODUCIBILITY, WHICH IS SO IMPORTANT WHEN TRYING TO QUANTIFY 5,000 GENE-METABOLISM INTERACTIONS."

To find out more about the Francis Crick Institute, visit **www.crick.ac.uk**

To find out more about the Charité – Universitätsmedizin Berlin, visit **www.charite.de/en**

To find out more about the SCIEX TripleTOF® 6600 System, visit **www.sciex.com/tripletof-6600-system**

Further reading

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FROM SOUP TO NUTS:

HOW ONE FOOD SAFETY LAB IS USING LC-MS TO DRIVE GROWTH

Julie Brunkhorst, Vice President of the Technical Division at Trilogy Analytical Laboratory

Trilogy Analytical Laboratory began life almost 20 years ago as a small start-up focused on mycotoxin analysis. It has since grown into an international enterprise and, today, the company offers an extensive portfolio of food and feed safety tests, relying on LC-MS technology for the analysis of a wide variety of sample matrices.

Trilogy Analytical Laboratory, based in Washington, Missouri, was established in 1999 by a team of five people – three owners and two chemists – who had previously worked together and decided to take the plunge and set up a laboratory of their own. The company initially focused on the analysis of mycotoxins – toxic metabolites produced by fungi – and has expanded to provide a range of food and feed safety analytical services that now includes drug residues and biogenic amines. Julie Brunkhorst, Vice President of the Technical Division, described how the company has evolved: "Trilogy began life in what was basically a very small garage, with minimal instrumentation – HPLC and GC – and a staff of five, one of them being me. From there, we have grown to a staff of around 25, with a laboratory that now operates 18 HPLC, two GC and three LC-MS systems. We handle a whole host of food products; in a typical week, we can analyze samples as simple as corn, wheat and barley, through to compound animal feed and human foodstuffs. Essentially, we test anything 'from soup to nuts', as the saying goes."

"We originally started with mycotoxin analysis because this was quite a niche market and we had expertise in this area. We knew the methodology, were familiar with the client base and had a lot of industry contacts. As the company grew, this expanded to include additional services, such as biogenic amines, drug residues and allergen testing. Some clients simply want to know whether a particular analyte meets the specified legal limit, while others want to know that their product is free from the slightest trace of allergens, such as gluten."

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Trilogy's relationship with SCIEX began in 2010, when the company invested in a refurbished API 3000™. Four years later, it acquired a SCIEX QTRAP® 5500 System, followed by a QTRAP 6500 System in 2016 and a QTRAP 6500+ in 2017. Julie continued: "The API 3000 was our first venture into LC-MS, but we didn't really embrace the technology until a client approached us about developing a method for the analysis of drug residues in urine, to ensure that it was antibiotic and growth promoter free. We worked with SCIEX to create an LC-MS method specific to the client's needs, and have since built on that to include additional drug residues."

"Instead of analyzing a sample using a GC and six different HPLC methods, we could run a single LC-MS protocol – it was simply a no brainer. This success created a drive to move most methods over to LC-MS technology, and we now have two instruments dedicated to mycotoxin analysis – the QTRAP 6500 and the QTRAP 6500+ – which are running seven days a week, almost 24 hours a day. And that's just mycotoxins! LC-MS gives us greater sensitivity and reduces the amount of sample preparation required, as the evaporation steps are limited, and derivatization is eliminated. We have also been able to move a lot of our sample preparation from immunoaffinity-based purification to solid phase extraction. This allows us to extract multiple analytes simultaneously, which is a considerable cost saving. Most of the samples we receive require multiple analyses – up to 20 different mycotoxins, for example – so we can be doing 300 LC-MS samples a day. We've even had to increase the capacity of our nitrogen tank, as our gas supplier couldn't keep up."

"Our SCIEX systems are ideal for our laboratory. We looked at instruments from other manufacturers but, in the end, it came down to the systems' small footprints and MultiQuant software. Having all SCIEX LC-MS systems gives us continuity and makes system set-up straightforward. When a new system is installed, it can be validated and in operation within a couple of days, as we don't need to wait for anyone to come and set up the methods. All of our LC-MS methods are quantitative, so the MultiQuant software is vital. It's easy to use and to train new staff, and we can customize it to suit our needs. It's just a wonderful tool for us. Another important purchasing consideration was technical support. We receive excellent support from our service engineer and know that if we do need help he will be with us within 24 hours, possibly even the same day. In addition, we can troubleshoot our systems remotely via online applications."

> "THIS SUCCESS CREATED A DRIVE TO MOVE MOST METHODS OVER TO LC-MS TECHNOLOGY."

"Before we had LC-MS, we were using a combination of HPLC, GC, and even thin layer chromatography, which was very time consuming. By implementing LC-MS, we have streamlined our workflows, reducing the work of two or three analysts down to one. It's saved us so much time. We are now even collaborating with another laboratory to develop an LC-MS method for biogenic amines, which will hopefully replace the HPLC assay currently in use," Julie concluded.

To find out more about Trilogy, visit **www.trilogylab.com**

To find out more about the SCIEX QTRAP 6500+, visit **www.sciex.com/qtrap-6500plus-system**

AN INCUBATOR FOR BIOPROCESSING EXPERTISE

Dr. Bi Xuezhi, Senior Scientist and Group Leader at the Bioprocessing Technology Institute

Biopharmaceuticals now account for a majority of new drugs entering the market globally, but the biomanufacturing processes required to isolate and purify these products are complex. Scientists at the Agency for Science, Technology and Research (A*STAR) in Singapore are using mass spectrometry to improve the understanding of bioprocessing methods, helping to improve the safety and efficacy of new biologics.

Singapore is fast becoming the biotechnology hub of Southeast Asia, with an ever-growing number of biotech start-ups sitting side-by-side with R&D facilities belonging to many global players in the life sciences and pharmaceutical markets. This concentration of biotech companies attracts personnel and expertise from across Asia and further afield, supported by government investment in education and training to ensure a workforce with the skills required to sustain this rapid growth.

Singapore's Agency for Science, Technology and Research (A*STAR) plays a key role in nurturing and developing this talent, as well as performing application-oriented research to advance scientific discovery and technological innovation. Dr. Bi Xuezhi, Senior Scientist and Group Leader in A*STAR's Bioprocessing Technology Institute, explained: "We are focused on drug discovery and development – primarily biologics – and undertake everything from the early phase candidate identification to batch production for preclinical studies. We perform a lot of in-house research but, because Singapore has so many biotech companies, we also participate in many collaborations, including large international projects. Our close ties with industry are further strengthened by our graduate and postdoctoral programmes, which mean that a lot of the people we now collaborate with have spent time working in the institute; we're an incubator for bioprocessing expertise!"

"This expertise, together with the wealth of multidisciplinary knowledge available across A*STAR, means that we also attract a lot of collaborations with larger companies," Dr. Bi continued. "Unlike small molecule drugs, which generally have a single effect on a specific target, biologics often have a far broader mode of action. This allows them to be active against various conditions – multiple cancers, for instance – but it also makes characterization of biopharmaceuticals far more complex. The nature of biosynthesis also means that there are likely to be trace amounts of biological contaminants in the purified biologics, and understanding exactly what these contaminants are is vital to the safety, efficacy and stability of the final product. For example, the presence of a protease in the purified drug will significantly reduce its stability. Likewise, if there is an immunogenic contaminant

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present, even in very small quantities, this could potentially cause a severe immune response."

"Any contaminating impurities must be identified and quantified, and most of the traditional methods are based on immunoassay techniques. These methods can be used to tell you the total amount of biological contaminants present, but cannot identify what these impurities are. Without knowing this information, it is very difficult to predict their effects on either the safety or stability of the product, or to improve the design of bioprocesses to eliminate these unwanted biomolecules. To overcome this issue, we use mass spec-based proteomics to fully characterize and refine bioprocessing workflows."

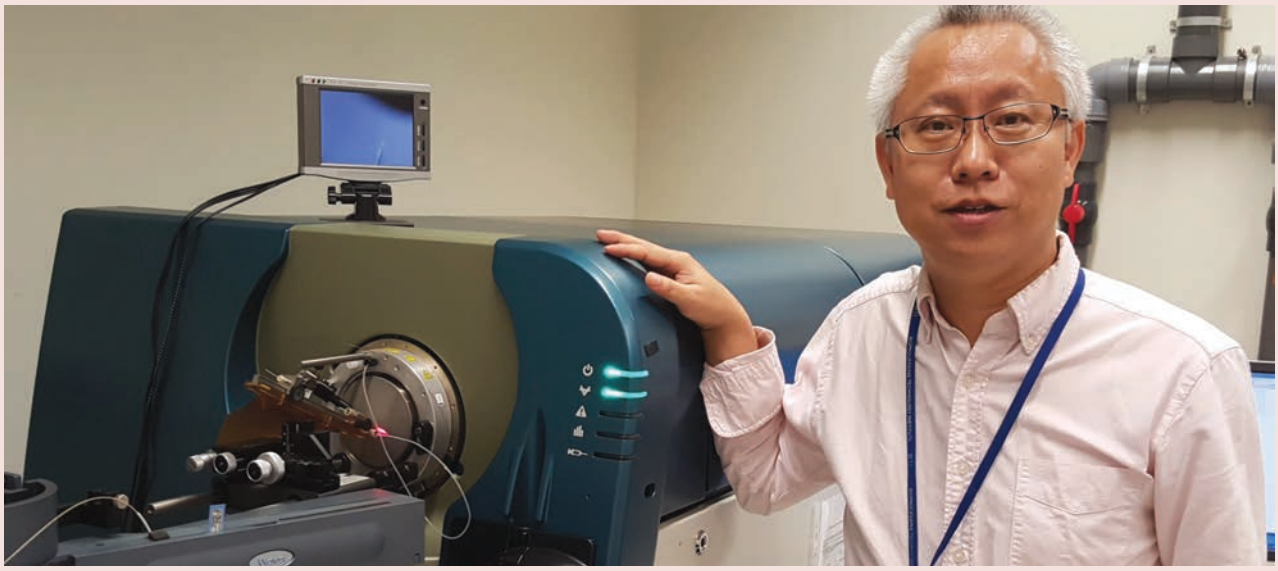
> "WE CAN NOW USE SWATH-BASED METHODS... TO SIMULTANEOUSLY MONITOR OVER 7,000 PROTEINS PER INJECTION."

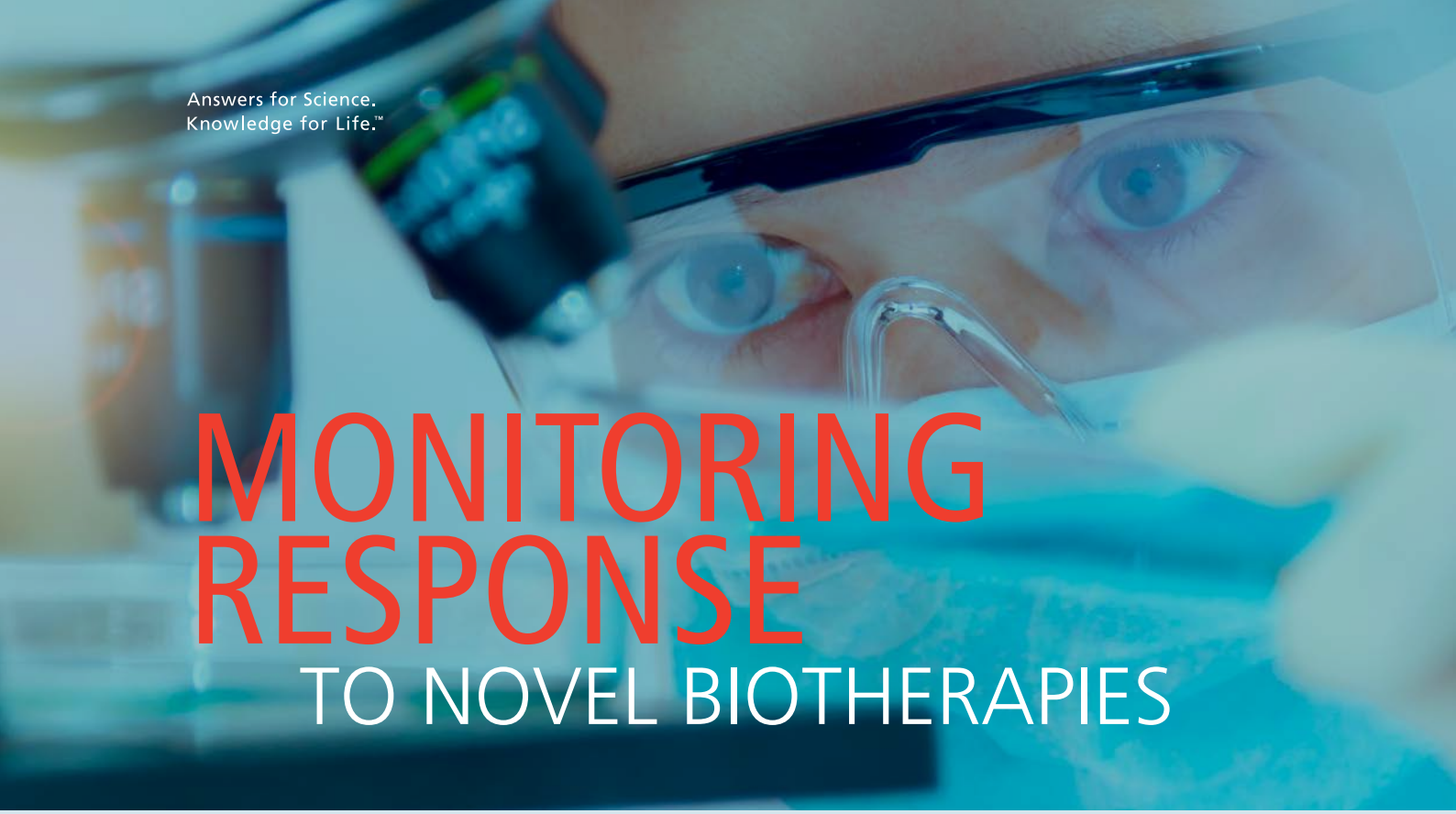
The depth of knowledge and skilled staff available in Singapore also make it an ideal location for scientific instrument manufacturers, with a number of companies – including SCIEX – choosing the country for both R&D and manufacturing facilities. Dr. Bi added: "We work closely with a number of MS instrument manufacturers, and have seen huge advances in MS technologies over the years. We currently have three SCIEX TripleTOF 6600 Systems in our lab, which have helped us to identify and eliminate impurities to refine our bioprocesses. The systems have also allowed us to perform SWATH Acquisition, which is fantastic for process characterization. Where we previously used isobaric labeling technologies and fractionation testing, we can now use SWATH-based methods. In collaboration with SCIEX, we have built up a comprehensive library of over 10,000 unique proteins – almost 140,000 peptides – from CHO cells, and can use this to simultaneously monitor over 7,000 proteins per injection. We have also worked with the company to develop robust and streamlined data interpretation tools specific to our needs, creating an extremely powerful solution for bioprocess analysis. Our biggest challenge now is ensuring robust and reproducible sample preparation to match the throughput of the system."

"Our collaboration with SCIEX aims to overcome some of the challenges faced by the biopharma sector globally. We want to push the boundaries of today's technologies, as well as to develop new hardware, software and applications that will address future needs," Dr. Bi concluded.

To find out more about A*STAR's Bioprocessing Technology Institute, visit **www.a-star.edu.sg/bti**

To find out more about the SCIEX TripleTOF® 6600 System, visit **www.sciex.com/tripletof-6600-system**





MONITORING RESPONSE TO NOVEL BIOTHERAPIES

The rise in immunotherapy is bringing fresh challenges to the monitoring of drug efficacy during clinical trials, prompting a need for new methods of detection and analysis. GlaxoSmithKline is turning to capillary electrophoresis-mass spectrometry to address one aspect of this, collaborating with SCIEX to develop unique methods for quantification of monoclonal antibodies.

Richard Snell, Investigator in the Bioanalysis, Immunogenicity & Biomarkers department at GSK

GlaxoSmithKline (GSK) is a global healthcare company engaged in research, development and manufacturing of pharmaceutical medicines, vaccines and consumer healthcare products. The company's pharmaceutical business specializes in therapeutic areas that include HIV, respiratory, oncology and immuno-inflammation, with a particular focus on research and development related to the immune system, the use of genetics, and advanced technologies.

Richard Snell, an Investigator in the Bioanalysis, Immunogenicity & Biomarkers department at the GSK site in Ware, UK, described the group's work: "I joined the company nearly 20 years ago while studying for a degree in applied biology with chemistry. At that time, the department was part of the drug metabolism and pharmacokinetics section, with the emphasis on small molecule LC-MS analysis for quantitative preclinical and clinical toxico- and pharmacokinetic studies, from first-in-human up to late-phase clinical trials. Today, the group is called bioanalysis, immunogenicity and biomarkers, and on the clinical side, we specialize in first-in-human studies. This work includes quantification of patients' responses to novel therapeutics, which usually involves in-depth method development and validation. We also analyze a lot of preclinical samples for both GLP and non-GLP studies, although these tend to rely on more generic set-ups. As well as our team in the UK, there is

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an equivalent group in the US. Both support studies of drugs being developed locally to minimize shipment of patient samples and, as we are analyzing similar types of molecules, we aim to have the same instrument capabilities across the two sites. Having the same lab systems, SOPs and regulatory standards gives us the flexibility to easily transfer methods between us if we need to."

Richard continued: "When I started at GSK, all the mass spectrometers were from SCIEX, and it has largely remained that way ever since. Currently, our instruments include API 5000s, Triple Quad 5500s and a TripleTOF 6600, as well as a CESI 8000 Plus capillary electrophoresis system. The Triple Quad systems are the workhorse instruments for the majority of our assays, particularly the small molecule studies, allowing us to quantify the drugs of interest and, often, metabolites or degradants as well."

> "I CAN SEE CESI BECOMING PART OF OUR LABORATORY ARMORY, GIVING US MORE OPTIONS AND AN ORTHOGONAL TECHNIQUE TO LC."

"Our most recent acquisition is the TripleTOF 6600, which gives us accurate mass capability. We've had the system for about 18 months now, and use it for more complex samples where we're seeing other peaks, as it gives us confidence that we are looking at the correct analyte. We can check for the isobaric and co-eluting metabolites that can easily catch you out, acquiring all the data upfront and mining it afterwards, rather than having to repeat the MS analysis. The system is also ideal for peptide mapping involving large molecule quantitation. Our aim is to transfer non-regulated quantitative work onto the TripleTOF because no infusion is required and there is very little set-up time. We are very impressed with the system's speed and sensitivity – to be able to scan at the speed it does without losing the sensitivity is quite impressive – and the Analyst software is far superior to other programs we have used."

"Capillary electrophoresis-electrospray ionization (CESI) is a new application for our lab; I first came across it at a SCIEX biologics conference. Although most of the applications discussed were for compound characterization, the technique showed good separation of large biotherapeutics and I felt that this approach might improve the quantitative methods employed for our monoclonal antibody studies. These methods rely on tryptic digestion of the antibodies to create a representative signature peptide for analysis. However, you can miss a lot of information by analyzing just one signature peptide of a few amino acids. CESI offered the potential for quantification of semi-intact molecules broken down into light and heavy chains, or intact antibodies. This provides far more information, for example, about possible modifications."

"We approached SCIEX about developing a CESI method for monoclonal antibody separation, and the company was very keen to collaborate with us. CE separations are not the same as LC and require a different mindset, but the CESI 8000 Plus is really easy to use and we've developed a method for one of our monoclonal antibodies that looks as if it will be fairly generic. That's a major advantage, as it will reduce the method development time for each new therapeutic, allowing us to focus more on the extraction protocols, which can be challenging. We're now working with SCIEX to develop and optimize electrokinetic injection – the application of a voltage to the sample to ionize the drug of interest, which then migrates up the capillary – replacing the hydrodynamic injection of a solvent containing the analyte and co-extracted compounds that is typically used for sample introduction. This effectively concentrates the analyte – under the right conditions it should be the only compound introduced to the capillary – reducing the potential for ion suppression by other molecules and improving sensitivity. The data so far is promising, with CVs around 8 %. I can see CESI becoming part of our laboratory armory, giving us more options and an orthogonal technique to LC," Richard concluded.

To find out more about GlaxoSmithKline, visit **www.gsk.com**

To find out more about the SCIEX CESI 8000 Plus, visit **www.sciex.com/cesi8000**

COMPOUND INTEREST: USING LC-MS TO EXPAND ANALYTICAL CAPACITY

Powerful analytical instrumentation is vital to the success of drug discovery research, enabling reliable characterization of a compound or metabolite without the risk of mistaking its identity. It also plays a crucial role in forensics, allowing laboratories to generate unequivocal information to support toxicology cases, such as potential drug-related deaths. The Division of Clinical Pharmacology at the University of Cape Town relies on the latest LC-MS technology to support the ever-expanding and diversifying analytical demands across both these sectors.

The Division of Clinical Pharmacology at South Africa's University of Cape Town (UCT) offers clinical and laboratory pharmacology services, as well as conducting both preclinical and clinical research focused on malaria, tuberculosis and HIV, including drug discovery and pharmacokinetic studies. In addition, it is involved in forensic toxicology and drugs of abuse screening. Over the last two decades, the division has invested heavily in mass spectrometry. Today, it has around 10 SCIEX systems, including ion trap and triple quadrupole instruments, and currently has the SCIEX X500R QTOF on loan as a demonstration instrument.

Dr. Lubbe Wiesner, Director of the UCT Pharmacology Research Laboratory, discussed his use of mass spectrometry: "MS is used for everything from initial compound exploration up to Phase III clinical trials, including pharmacokinetic studies. We mainly use the QTRAP systems in our drug discovery and development program, as they are good instruments for early identification of metabolites of new compounds. The triple quadrupole systems are mostly used for pharmacokinetic investigations, but they are also indispensable for training. I supervise about 15 postgraduate students, who gain hands-on experience of MS using these instruments. They start off using the older systems and then, as they improve their practical skills, move on to the newer, more sensitive instruments."

The most recent addition to the lab is an X500R QTOF System which, since its installation in October 2017, has been processing much of the laboratory's alternative workload. Alicia Evans, Manager of the Mass Spectrometry Toxicology Laboratory, explained: "A few years ago, we offered a preliminary drug screening service to UCT's Forensics Department to try to alleviate some of the pre-existing backlogs. We offered a quick turnaround time for samples received for cases which were possible drug-related deaths, and the pathologists have found the service really useful."

"Initially we used a 3200 QTRAP System for this work but, when we heard about the release of the X500R, we immediately got in touch with Separations, the South African distributor for SCIEX. We had heard good things about the instrument's potential and particularly its ease of use for drug screening using the SCIEX vMethod. The column and mobile phases are predetermined in this method, and the retention times of 664 compounds have already been established. Another reason for choosing the QTOF was its high resolution capabilities; it is better at differentiating between similar compounds, which can significantly reduce false positive results."

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Dr. Lubbe Wiesner, Director of the Pharmacology Research Laboratory at the University of Cape Town

Lubbe continued: "The ability to distinguish between subtle differences in molecular structure is also vital to early drug discovery – when you are elucidating chemical structures, you need high resolution to determine chemical formulae – and you can do so much more with time of flight instruments. One of our students, who is working in early drug discovery targeting malaria, used the X500R to successfully characterize the chemical formulae of two new compounds. These were isolated and tested against malaria, and their activity was comparable with drugs currently being used in the clinic. We're very excited about the QTOF – it's amazing what it can do."

> "WE'RE VERY EXCITED ABOUT THE QTOF – IT'S AMAZING WHAT IT CAN DO."

MS has also proved beneficial for confirmatory testing undertaken for private forensic testing laboratories across the country. "Toxicology analysis in South Africa often relies on off-the-shelf immunoassay kits and simple dipstick tests. On many occasions, when the same samples have been run on one of our MS systems – initially a Triple Quad, but now the QTOF – we have found that, in fact, the immunoassays show a degree of cross-reactivity. This is highlighted by differing immunoassay and MS results; the compound originally identified by immunoassay may actually be a spurious result due to interference or a completely different compound. Our MS capabilities have helped a lot with confirmatory testing, as we can be certain that the compound reported has been correctly identified," said Alicia. "We've also used the QTOF system to analyze some influent and effluent water samples from a nearby wastewater treatment plant in Cape Town as part of an academic project. Other projects planned will include the analysis of wastewater for antiretroviral and TB drugs."

"The nice thing about the vMethod is that it includes a lot of metabolites and not just parent compounds. It really reassures you that you are detecting the right thing. At the moment, most of our work on the QTOF is qualitative – a compound or metabolite is either detected or it is not. We have the capability to set up quantitative assays in the future, but the X500R has been very busy since it was installed in October – we've definitely put it to good use," Alicia concluded.

To find out more about the University of Cape Town's Division of Clinical Pharmacology, visit **www.medicine.uct.ac.za/med/divisions/pharmacology**

To find out more about the SCIEX X500R QTOF System, visit **www.sciex.com/x500r**

Answers for Science.
Knowledge for Life.™

SELEXION®

DIFFERENTIAL MOBILITY SEPARATION TECHNOLOGY FOR THERAPEUTIC BIOANALYSIS

Jeff Plomley, Manager and Principal Scientist at Altasciences

In the early stages of drug development, biopharmaceutical companies often rely on specialist analytical services to develop methods for assessing new therapeutics. Quebec-based Altasciences is using SCIEX SelexION technology to improve the performance of drug monitoring and meet the needs of its clients' increasingly patient-centered approaches.

Altasciences is a contract research organization with over 25 years of experience providing early drug development services – from discovery to proof of concept – for biotechnology and pharmaceutical companies globally. Headquartered in Quebec, Canada – with additional facilities in Kansas City (Kansas), Fargo (North Dakota) and Seattle (Washington) in the USA – the company offers a wide range of bioanalytical services to support drug development, from preclinical studies through to Phase IV trials. Jeff Plomley, Manager and Principal Scientist for LC-MS method development and innovation, explained: "The variety of work my team supports varies greatly, with many distinct R&D projects running at any given time. The lab supports both small and large molecule applications for preclinical and clinical programs, and we're always looking out for new technologies or workflows that can progress our bioanalytical services to better assist our customers."

"For example, one of the emerging technologies our clients are increasingly asking us to support is volumetric absorptive microsampling (VAMS), a novel technology enabling precise and effective collection of a single drop of blood (around 10 µl). This is very attractive to the industry, as it is both easy to use and patient friendly, making it well suited to pediatric use and home-based sampling. Being only minimally invasive, it also helps to reduce animal welfare concerns in preclinical studies. We have therefore invested heavily in our expertise and workflows to support VAMS, developing an impact-assisted extraction technique to overcome hematocrit-associated issues and optimize sample recovery."

"We have 33 SCIEX mass spectrometers in operation on a daily basis – including API 3000, Triple Quad 5000, Triple Quad 5500, QTRAP 5500 and TripleTOF 5600+ and 6600 systems – with a throughput of about 720,000 samples per year," Jeff continued. "The advanced capabilities of our newer SCIEX Triple Quads have been instrumental in overcoming some of the common problems associated with LC-MS-based drug monitoring applications. For example, we have made big strides in monitoring anti-epileptic drugs (AEDs) – an essential activity for clinical trials of new drugs and optimization of individualized, combined AED therapies. AEDs offer numerous challenges for LC-MS workflows:

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some fail to fragment or fragment inefficiently under MS/MS conditions, others may only ionize effectively in one polarity mode of electrospray, and large disparities in LogP values can make it a challenge to retain the most polar analytes while minimizing overall run time. These hurdles mean that most workflows rely on two separate LC-MS assays. Instead, we are using functions such as dynamic polarity switching and scheduled MRM to overcome these challenges, allowing us to monitor a panel of 16 AEDs in a single assay that takes just six minutes, which is quite a breakthrough."

"The small sample volumes associated with VAMS make it more important than ever to have high sensitivity mass spectrometers – an area where SCIEX has always led the field – and so we've also recently purchased three Triple Quad 6500+ instruments for our microsampling and biomarker initiatives. These systems are equipped with SelexION differential mobility separation (DMS) technology, which has been instrumental in helping us to overcome selectivity challenges, or when we need very low detection limits and baseline noise needs to be minimized."

> "I CANNOT IMAGINE A BIOANALYTICAL LAB OF THE FUTURE THAT DOES NOT HAVE THIS TECHNOLOGY."

"SelexION is particularly useful when we encounter isobaric interferences that are difficult to resolve chromatographically or by sample preparation approaches. For example, when analyzing hemolyzed samples to determine the concentration of allopurinol – a drug used to lower uric acid levels in blood – we have been able to eliminate endogenous isobaric interference from hypoxanthine, a naturally occurring structural analog which is present in much higher abundance than allopurinol. Without DMS, this would have required exhaustive sample preparation and prolonged chromatographic separation, which would have significantly limited assay throughput. SelexION technology has also been useful for lowering the limit of quantitation (LOQ) achievable for fingolimod, an immunomodulatory drug for multiple sclerosis. We were already at the LOQ of our previous method – 20 pg/ml – but a client required an LOQ of just 5 pg/ml. Using DMS we were able to significantly reduce the background noise to achieve this four-fold improvement in LOQ, something that would have been exceptionally difficult, if not impossible, to do otherwise."

"As well as overcoming chromatographic challenges, SelexION has been invaluable for reducing the amount of sample preparation required for many of our assays. We have used this technology to help remove detection-limiting interference for a number of large molecule quantitation applications, such as rituximab monitoring. Rituximab – which is used to treat several autoimmune diseases and cancers, eg. non-Hodgkin lymphoma – can now be extracted using a very crude, rapid but non-selective sample preparation approach, combining the superior sensitivity of the Triple Quad 6500+ instruments with SelexION DMS to exclude interfering species and minimize baseline noise. We've achieved similar selectivity and better sensitivity compared to our previous methods, with far less sample preparation."

"At the other end of the spectrum, SelexION is being used for low molecular weight tobacco biomarkers in urine, where the highly complex and variable matrix can lead to significant interference. For one biomarker, we have removed the requirement for 2D chromatography and orthogonal SPE by using SelexION. This has significantly reduced consumables costs and increased sample throughput, so the technology will pay for itself over time. Having applied SelexION DMS to a plethora of LC-MS challenges and seen the benefits – from the elimination of interference to the improvements in LOQs – I cannot imagine a bioanalytical lab of the future that does not have this technology. It's such a universal approach for achieving gains in both selectivity and sensitivity," Jeff concluded.

To find out more about Altasciences, visit **www.altasciences.com**

To find out more about SCIEX's SelexION technology, visit **www.sciex.com/selexion**

Prof. Dr. Guowang Xu, Director of the CAS Key Laboratory of Separation Science for Analytical Chemistry at the Dalian Institute of Chemical Physics

DEVELOPING A PSEUDO-TARGETED MS METHOD FOR METABOLOMICS

Researchers at the Dalian Institute of Chemical Physics have a keen interest in the development of novel mass spectrometry-based methods for metabolomics. Building on years of experience in the field, the Chinese team has established an innovative pseudo-targeted strategy that has been successfully applied to metabolomics and lipidomics studies.

The CAS Key Laboratory of Separation Science for Analytical Chemistry at the Dalian Institute of Chemical Physics (DICP), part of the Chinese Academy of Sciences, is devoted to research and development of novel analytical methods and techniques for complex systems and metabolomics. Led by Director Prof. Dr. Guowang Xu, the group's recent focus has been on the development of multidimensional chromatography platforms for metabolomics and their applications in disease and drug research, particularly traditional Chinese medicine. Professor Xu discussed the team's work and the changing face of metabolomics: "Metabolomics is the systematic study of organisms' response to internal gene mutations, pathophysiological changes or external environmental stimuli. Since I began working in this field in 1996, metabolomics has developed tremendously, with mass spectrometry and nuclear magnetic resonance contributing significantly to this advance."

He continued: "Liquid chromatography-mass spectrometry (LC-MS) is an increasingly important tool in metabolomics. It can be used for disease classification and biomarker discovery, and for applications in pathophysiology, monitoring diagnostic biomarkers of disease, food safety, environment and medical research. It will play a progressively more important role in precision and translational medicine, as well as many other fields."

Most recently, the team has focused on two main areas of research: 1) the continuous expansion of its in-house LC-MS/MS database to improve the metabolite identification, and 2) the development of a novel pseudo-targeted MS method to better serve clinical research into metabolomics. "Metabolite identification is one of the biggest bottlenecks in metabolomics studies," said Professor Xu. "High resolution MS can acquire tens of thousands of fragment ions from a single injection of a sample, but ultimately it may only be possible to identify a few hundred metabolites. This led us to establish an in-house metabolite database, taking advantage of the highly efficient MS/MS acquisition capabilities of the SCIEX TripleTOF 5600 System, which played an important role in this study. The database now includes almost 7,000 metabolites, and that number is still growing."

Metabolomics is mainly divided into non-targeted and targeted analysis strategies, but Professor Xu's team has developed a novel pseudo-targeted method that combines the advantages of the comprehensive coverage of non-targeted, full scan acquisition with accurate quantification by targeted multiple reaction monitoring (MRM). "Pseudo-targeted metabolic profiling comprises three steps; non-targeted profiling by quadrupole time-of-flight MS, selection of precursor/product ion pairs, and MRM analysis of these transitions using a triple quadrupole or QTRAP MS system – the instruments of choice for quantification studies."

"In contrast with multiple targeted metabolomics, a pseudo-targeted method provides global metabolome information with the aid of real samples, rather than only identified metabolites. This eliminates dependence on reference standards, simplifies the optimization of subsequent MRM analysis, and can detect both known and unknown metabolites at the same time, significantly expanding coverage. Our TripleTOF 5600 and QTRAP 5500/6500+ systems contributed a lot to the development of the pseudo-targeted method, allowing us to expand the list of metabolites screened from a few dozen to a few hundred, or even one or two thousand. Compared to non-targeted methods, pseudo-targeted analysis offers good sensitivity, improved repeatability and a linear range of four to five orders of magnitude. We have also applied this strategy to our lipidomics research, acquiring an MRM ion pair list in excess of 3,300, including more than 7,000 lipid compounds."

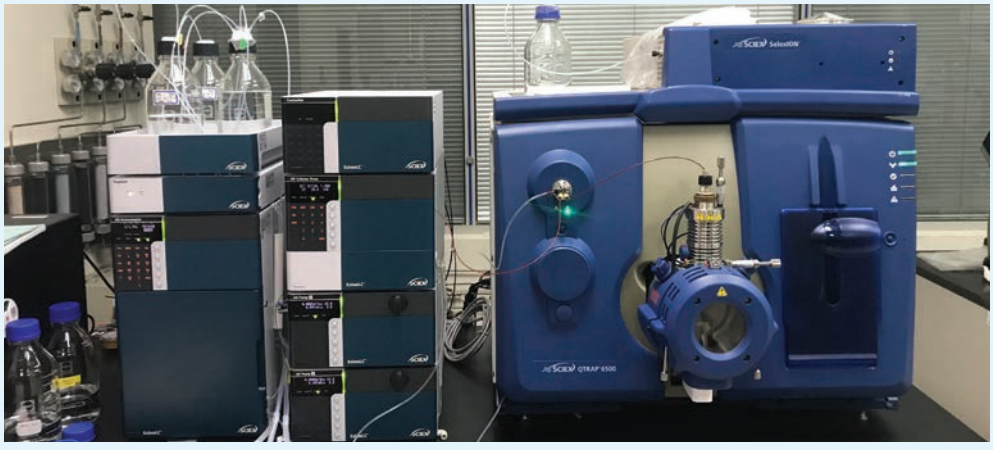
To meet the need for good reproducibility over a prolonged period during large-scale clinical research studies, the group integrated a blank wash and a pooled quality control sample into the pseudo-targeted method. Post-run calibration was also included. This ensures excellent stability, allowing large numbers of samples – at least 282 injections, with a runtime of about 110 hours – to be analyzed on the QTRAP systems with minimal intervention between batches. "This approach greatly improves the efficiency of analysis of clinical samples, helping research into precision medicine and clinical diagnostics, and we've used it for more than 1,000 samples across several cohort studies. For example, we analyzed samples from 1,448 subjects in a study of hepatocellular carcinoma, and identified two potential metabolic biomarkers for early diagnosis of the disease; phenylalanyl-tryptophan and glycocholate. This led to the development of a kit for the detection of glycocholate using LC-MS – recently licensed for clinical use by the Zhejiang Food and Drug Administration."

> "THIS LED US TO ESTABLISH AN IN-HOUSE METABOLITE DATABASE, TAKING ADVANTAGE OF THE HIGHLY EFFICIENT MS/MS ACQUISITION CAPABILITIES OF THE SCIEX TRIPLETOF 5600 SYSTEM."

"When you are running large-scale studies, the MS instruments need to be in operation 24 hours a day, all year round. It is important that your systems are robust and reliable. The SCIEX mass spectrometers are a real asset to our work and, just as importantly, we receive excellent service and support from the company," Professor Xu concluded.

To find out more about the Dalian Institute of Chemical Physics, visit **english.dicp.cas.cn/au/bi**

To find out more about the SCIEX TripleTOF® 5600+, visit **www.sciex.com/tripletof-5600**



DELVING INTO THE PATHOLOGY OF NEUROLOGICAL AND IMMUNOLOGICAL DISEASE

Ludovicus Staelens, UCB's Head of Bioanalysis for Belgium

Understanding the underlying molecular pathology of a disease at the molecular level is key to developing effective therapies. Global biopharmaceutical company UCB focuses on the discovery and development of novel therapies in two key areas – neurology and immunology – and uses multiple SCIEX systems to analyze the differing roles of small and large molecules in a range of conditions.

Advances in the sensitivity, selectivity and throughput of the technologies used to study molecular pathology are giving researchers a better understanding of the mechanisms behind disease, helping to uncover new therapeutic targets that improve the longevity and quality of lives. Since its establishment in 1928, UCB has undergone a major transformation from a speciality chemical company into a global biopharmaceutical business. The company now focuses on developing therapies for neurological and immunological diseases, covering a broad range from epilepsy and Parkinson's to arthritis and lupus. Research is performed across two main sites; one based in Slough, UK, and another in Brussels, Belgium. Ludovicus Staelens, Head of Bioanalysis for Belgium, is responsible for the development and validation of bioanalytical methods, and subsequent sample analysis for both small and large molecules. He explained: "Originally, we only performed GLP and non-GLP bioanalysis of small molecules. However, when we started doing GLP work on large molecules, it was much easier to outsource regulated small molecule work that the lab simply didn't have time to perform anymore. Today, we still conduct non-GLP small molecule bioanalysis, while our regulated labs perform preclinical and clinical analysis up to Phase I trials on large molecules – any other work is outsourced."

"Although the assays we conduct can vary from project to project, there are specific assays that we routinely run – every study will have a pharmacokinetics analysis and most will also have an anti-drug antibody analysis – and each of these methods is custom developed for the individual project. The core technologies of our work are ligand binding assays (LBA) for large molecule work and LC-MS/MS – which we started using at the end of the nineties – for both the large and small molecule studies. When we started conducting mass spec analysis of large molecules, the application and workflow changed substantially, although the technique itself did not. We have three SCIEX API 5000 triple quadrupole platforms that we use for analysis of *in vitro* samples because of their robustness. For applications that require higher sensitivity and selectivity, we use the Triple Quad 6500 for small molecules, and the Triple Quad 6500+ for large molecules. The Triple Quad 6500+ is excellent for high sensitivity protein analysis because we can combine it with immunocapture approaches to achieve very low limits of quantification. We use a bottom-up approach

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for large molecule analysis, because you lose a lot of sensitivity when analyzing full proteins as a result of charge and isotopic signal dispersion. Digesting the protein of choice and selecting a signature peptide as a surrogate avoids these issues and gives improved sensitivity."

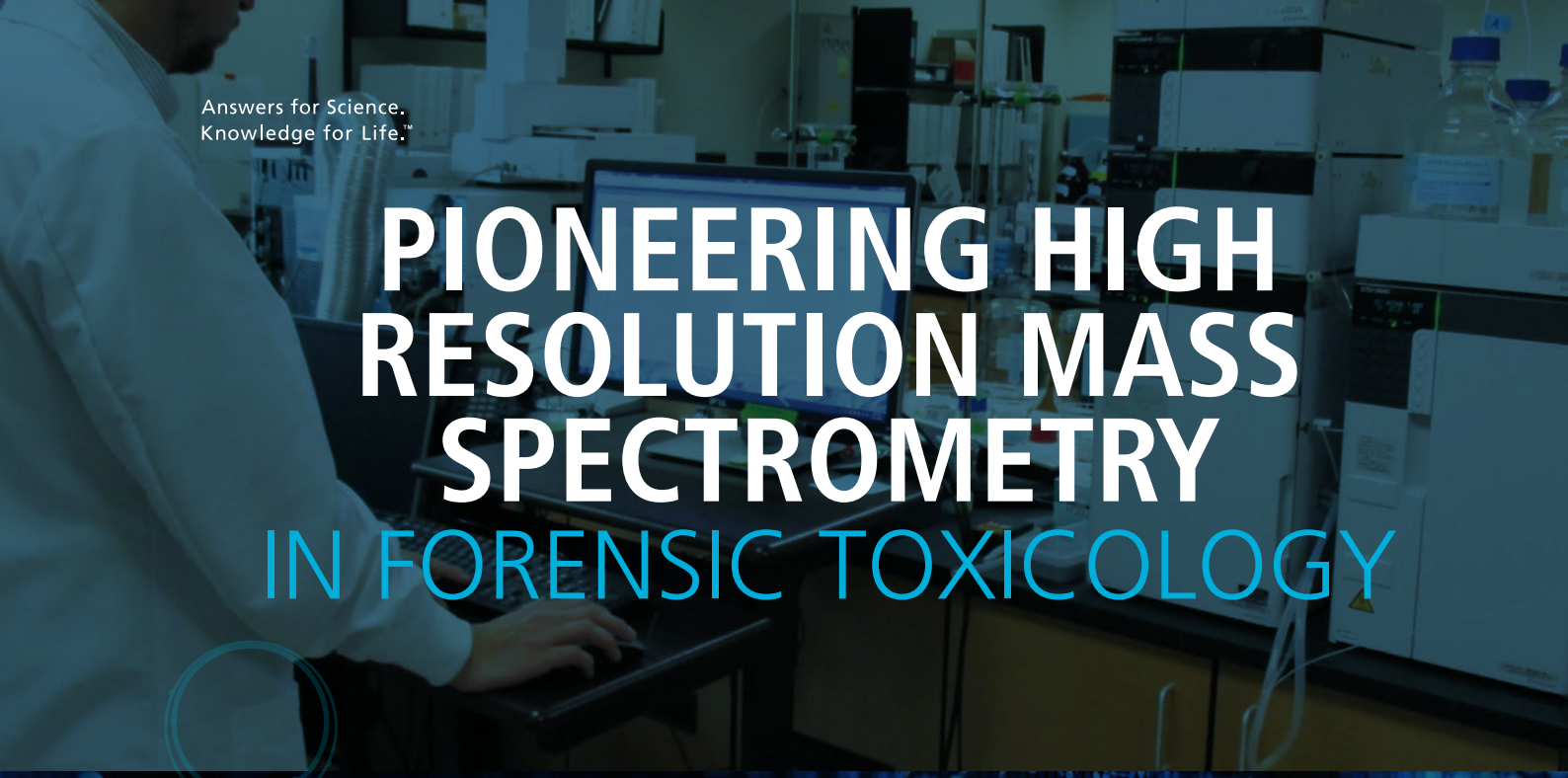
"The majority of our work is actually assay development – just about all of our method development is done in house. It's a really important field, because our contributions can greatly assist outsourcing once clinical studies progress to Phase II; at that stage, the technology transfer is critical. The Triple Quads are well suited to this work, because they are really powerful and more robust than other systems, and require little maintenance, even when running almost continuously. In addition, they are widely available at our partner CROs. We use the MultiQuant software for integration because it enables us to easily set up integration parameters so that we can process our entire run in one go; we're not allowed to change settings from one injection to the next in our regulated work, and this software makes integration easy. It doesn't usually require any adjustments after the first set-up, which saves time, and it's regulatory compliant. We also use a variety of other software applications for method development, and it's easy to link these to the SCIEX systems. This versatility extends to the systems' compatibility with a range of LC platforms, which allows us to alter our set-up dependent on our current needs."

"As technology continues to improve, the industry as a whole is moving towards the use of high resolution platforms, such as the TripleTOF 6600. These systems offer increased selectivity alongside supplementary possibilities in protein analysis, and we will be investigating this technology further, as it may be hugely beneficial to our method development work," concluded Ludovicus.

To find out more about the work of UCB, visit **www.ucb.com**

To find out more about the SCIEX Triple Quad™ 6500+ system, visit **www.sciex.com/triple-quad-6500plus-system**

> "THE TRIPLE QUAD 6500+ IS EXCELLENT FOR HIGH SENSITIVITY PROTEIN ANALYSIS BECAUSE WE CAN COMBINE IT WITH IMMUNOCAPTURE APPROACHES TO ACHIEVE VERY LOW LIMITS OF QUANTIFICATION."



PIONEERING HIGH RESOLUTION MASS SPECTROMETRY IN FORENSIC TOXICOLOGY

Forensic toxicology is a discipline that combines the principles of toxicology with other fields – such as pharmacology and analytical chemistry – to support legal investigations into poisoning, drug abuse and causes of death. Access to sensitive and reliable analytical instruments is essential for a forensic laboratory to defend results in a legal setting, which led Oregon State Police to adopt pioneering high resolution mass spectrometry technology for its routine screening operations.

The Oregon State Police department is well served by two toxicology labs in Portland and Springfield, USA. These labs offer forensic services for police investigations and analyze evidence in criminal cases. Sara Short, Toxicology Technical Leader, described their workload: "We mainly perform driving under the influence of intoxicants (DUII) analysis – assessing drivers who are suspected to be impaired – and post-mortem toxicology testing for the Oregon State Medical Examiner, aiding them in determining causes of death. In addition, we have an implied consent program involving breath alcohol testing."

"We process around 5,000 DUII and 4,700 medical examiner requests every year, working mostly with body fluids – blood, urine and vitreous humor from the eye – or, if a body is significantly decomposed, we may perform toxicology analysis on the gastric contents, spleen or liver tissue. We were using immunoassays and GC-MS for our screening, followed by quantitative analysis for our post-mortem samples on a SCIEX 3200 QTRAP System, which we have owned for the past 10 years. However, there was a need to increase the speed and sensitivity of the screening process, and we decided to purchase a high resolution mass spectrometry instrument, which we heard about at the Society of Forensic Toxicologists (SOFT) meetings."

Michael Jackson, an analyst in the lab, added: "To help us decide which system to purchase, we generated samples spiked with certain drugs, and sent them to a number of suppliers to compare and contrast various instruments. The SCIEX TripleTOF 5600+ System really outperformed the other instruments, obtaining fewer false positives and false negatives, and the reported concentrations of the analytes were closest to our target concentrations. In addition, we were already familiar with the software, having used the SCIEX 3200 QTRAP System, so there was a shorter training curve for analysts if we adopted a second instrument from the same company."

After purchasing the SCIEX TripleTOF® 5600+ System, the Portland lab needed to carry out preliminary tests to validate the instrument, as Sara explained: "I worked closely with the quality assurance manager to devise a validation plan that would rigorously test the sensitivity, reproducibility, and robustness of this technology for the toxicology section. The validation was completed in October 2017, and we achieved a limit of detection of 10 ng/ml for most drugs, while some were detected as low as 1 ng/ml. As part of the validation process, we added 96 drug standards to one blood sample to evaluate interferences from commonly encountered analytes; the system could detect over 90 % of those

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Michael Jackson, Laboratory Analyst, and Sara Short, Toxicology Technical Leader, at Oregon State Police

drugs. The instrument not only has a high resolution, it also has the ability to separate analytes based on retention time. The lab in Springfield carries out the same work, except for post-mortem toxicology, and when it installed an identical instrument at the end of July 2017 we were able to complete the validation far more quickly. We set up a comparative study between the labs, and repeated a limit of detection study for both instruments to highlight any variability."

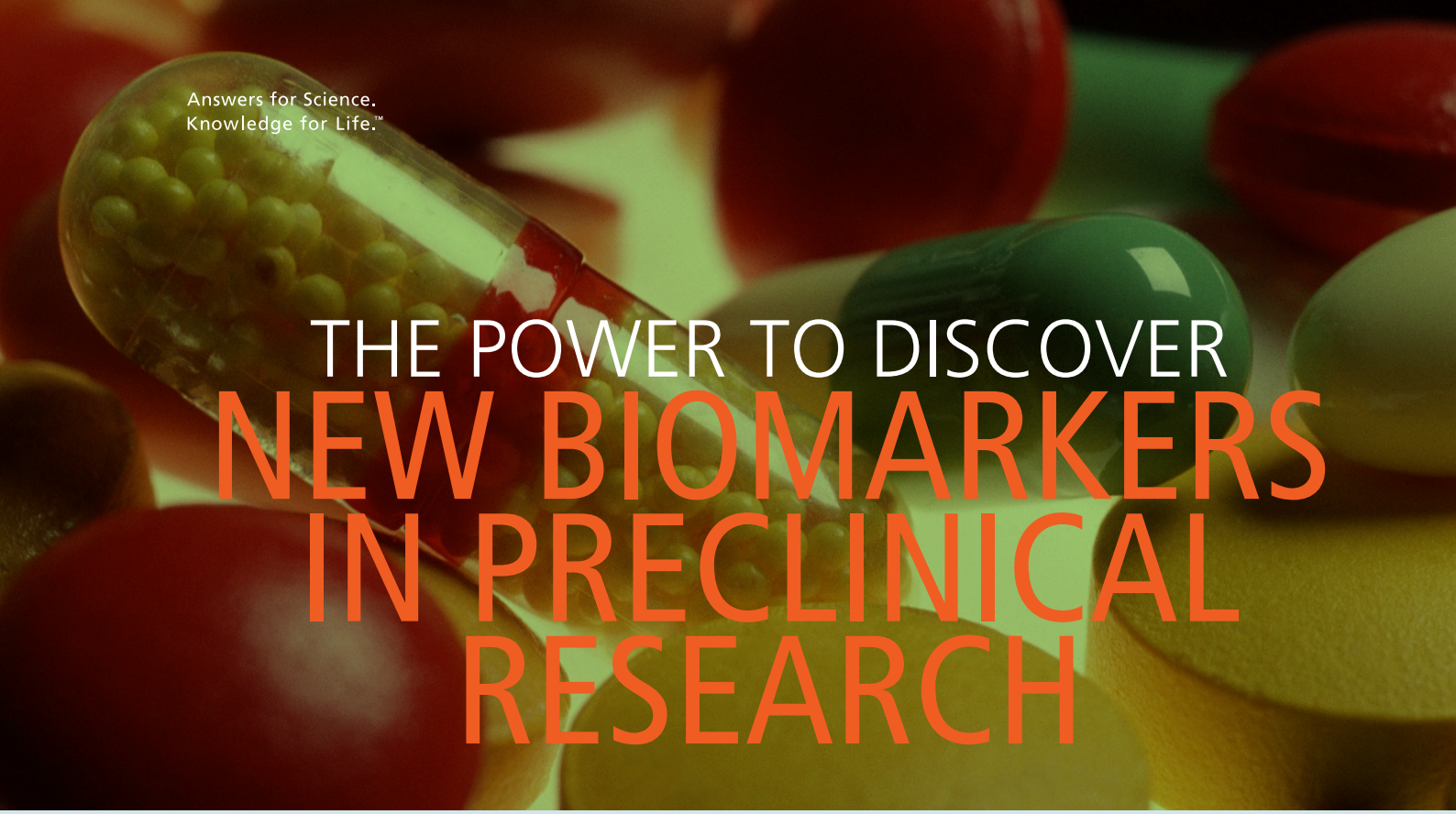
"High resolution mass spectrometry has brought a number of benefits," Sara continued. "For starters, when we compared the old methodology to the new, we had no false positives and could see additional metabolites due to the improved instrument sensitivity. We are also extracting our samples in a different way, using dilution and direct injection for urine samples instead of solid phase extraction (SPE), which was time consuming and required large volumes of solvent and urine. For blood samples, we are using a supported liquid extraction procedure that's very fast and clean, and replaces SPE, saving us time and hopefully money in the long run. We can now obtain masses of compounds up to five decimal places, in contrast to the nominal masses from GC-MS. In addition, having two complementary but different technologies provides further confidence to our findings; using the SCIEX TripleTOF 5600+ System as our initial screening instrument, followed by the SCIEX 3200 QTRAP System for quantification, satisfies criteria from the SOFT guidelines and our own procedures. It also helps to support our findings when presenting in court. In addition, we have switched over to the TripleTOF system's SWATH Acquisition capabilities. If you have multiple analytes eluting from your LC column at the same time, the instrument is able to use SWATH analysis to separate the data to ensure you are observing a true analyte. It holds a lot of promise, particularly in the rapidly changing illegal drugs market; we should be able to look at previously undetermined causes of death and cross-reference the recorded data with new drugs as we identify them."

> "…THE CUSTOMER SUPPORT HAS BEEN OUTSTANDING AND I CAN'T SAY ENOUGH POSITIVE THINGS ABOUT IT."

Michael concluded: "We've been very impressed with the technical support from SCIEX. We've experienced an extremely steep learning curve with this new technology, and any time I've had a question, I've felt comfortable sending an email to the company. It's not uncommon to receive a reply by the next, if not the same, day. Should we have an issue with the instrument, the SCIEX team can connect to it remotely, review the data and help troubleshoot the situation. It's very reassuring; the customer support has been outstanding and I can't say enough positive things about it."

To find out more about the Oregon State Police forensic division, visit **www.oregon.gov/osp/programs/forensics/Pages/default.aspx**

To find out more about the SCIEX TripleTOF 5600+ system, visit **www.sciex.com/tripletof-5600**



THE POWER TO DISCOVER NEW BIOMARKERS IN PRECLINICAL RESEARCH

Dr. Naoto Senda, Senior Director of the Tsukuba Bioanalysis Laboratory at SNBL

High sensitivity detection and analysis of biomarkers and other molecules is critically important during preclinical trials. Researchers at Shin Nippon Biomedical Laboratories (SNBL), one of the biggest contract research organizations in Japan, depend on SCIEX LC-MS/MS technology to conduct a variety of pharmaceutical projects.

SNBL was established in Kagoshima in 1957 and has, since then, opened numerous offices and facilities throughout Japan and Asia. It is the only company in Japan capable of performing the appropriate tests necessary for all stages of drug development, providing research and development services for a range of disease areas.

The Tsukuba Bioanalysis Laboratory – set up in 2015 and led by Senior Director Dr. Naoto Senda – is the Preclinical Research Support Division for SNBL, conducting equal numbers of contract research and internal projects. Researchers at the Tsukuba laboratory use LC-MS/MS to develop ultra high sensitivity methods for quantitative measurement of proteins, peptides, nucleic acids and extremely low molecular weight compounds as relevant biomarkers or potential drugs. Dr. Senda explained: "We develop mass spectrometry-based methods for measuring target molecules at high sensitivities, and rely heavily on SCIEX instruments for our work. Until recently, many contracts focused on quantifying the drugs themselves, but we are now mainly looking at disease-specific biomarkers that relate to drug efficacy and safety; it has become increasingly common for pharmaceutical companies to ask for these kinds of markers to be measured. We are also frequently working with nucleic acids (which have recently become popular candidates as potential

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drugs), cyclic peptides, monoclonal antibodies and V_HH antibodies – a specific sort of antibody with a much smaller molecular weight than usual."

The Tsukuba group has a very specific workflow strategy, as Dr. Senda described: "Our analytes are often proteins, and we use a SCIEX TripleTOF 5600+ System, equipped with an Eksigent ekspert nanoLC 400 system, for exact mass analysis. We use SWATH Acquisition and ProteinPilot software to identify and quantify characteristic proteins by exact mass, sometimes followed by sample comparisons using MarkerView to find any treatment effects. The ion transitions found by exact mass are then put through nominal mass analysis, using our two Triple Quad 5500s or our QTRAP 6500+. We use this data to build up ultra high sensitivity methods." Mass spectrometry is a key technology for several SNBL sites; there are seven SCIEX instruments at the Drug Safety Research Laboratories in Kagoshima, and another 28 at the Pharmacokinetics and Bioanalysis Center in Wakayama. Once developed, the measurement methods optimized by Dr. Senda's team are transferred to these laboratories for the analysis of larger numbers of samples.

> "…THE SWATH ACQUISITION, AS WELL AS THE MARKERVIEW AND PEAKVIEW SOFTWARE SOLUTIONS [ARE] EXTREMELY USEFUL; THEIR OPERABILITY IS BRILLIANT AND IT IS EASY TO UNDERSTAND STRAIGHTAWAY WHETHER A BIOMARKER HAS BEEN UP- OR DOWN-REGULATED."

Dr. Senda has over 30 years of experience in the technique, including 20 years' familiarity with SCIEX instruments. He has been particularly impressed with the high sensitivity and the intuitive software that SCIEX mass spectrometers provide. "We are very grateful for our Triple Quad 5500 systems, which serve as workhorse instruments for our nominal mass work," he said. "We find the SWATH Acquisition, as well as the MarkerView and PeakView software solutions to be extremely useful; their operability is brilliant and it is easy to understand straightaway whether a biomarker has been up- or down-regulated. We also have SelexION+ on our QTRAP 6500+, which has turned out to be extremely helpful for the analysis of nucleic acids."

With so many instruments and a challenging workflow, the technical support from SCIEX has been invaluable. Dr. Senda added: "SCIEX's service organization is very strong; if we ever need advice, we can contact the specialists by phone and, if necessary, the engineers will arrive to help us on the following day. We highly value this level of support, which helps us to continue our work with the minimum of downtime."

To find out more about SNBL, visit **www.snbljapan.com**

To find out more about the pharma and biopharma applications of SCIEX systems, visit **www.sciex.com/applications/pharma-and-biopharma**

BUILDING THE BEST OPERATIONS TEAM FOR OUR CUSTOMERS

JACK TUEN, VICE PRESIDENT, GLOBAL OPERATIONS, SCIEX

How being the best operations team in Danaher is critical to the success of our customers, SCIEX and our associates.

Our operations team is an integral part of our core business and, without it, our products wouldn't be manufactured and delivered to our customers in a timely fashion. It is the team's mission to continue striving to become the best operations team across Danaher, building on our strong Danaher Business System (DBS) principles and constantly learning from the best practices of other similar organizations.

The core purpose of our team is to enhance customer experience by providing high quality and reliable products that they trust, delivered on time, and offered at a competitive cost. To do that, we focus on implementing and predicting our operations – 'keeping the trains on time, all the time.' Our DBS principles have provided a solid foundation and, from there, we will embark on an exciting journey to achieve our Mission 2020 – to build an organization that attracts talented people who will be proud to be part of SCIEX.

Our customers need:

- SCIEX products that are easy to order, install and use
- Reliable delivery, quality and operation, with high instrument uptime
- High level product performance

Our success in carrying out our quality, delivery and productivity plans ensures that we deliver value to our customers as promised, helping them to succeed in advancing scientific understanding and safeguarding health. Our high performance and reliability in meeting customers' expectations is the hallmark of the SCIEX brand – the foundation of everything we do, and the reason we do it.

By becoming the best, SCIEX helps to improve the performance across Danaher operations and foster a culture of healthy competition, collaboration and continuous improvement. We create a high performing team by constantly driving breakthrough improvements that continue to challenge the status quo and seek out-of-the-box ideas through Kaizen and benchmarking initiatives.

SCIEX strives:

- To differentiate itself from its competition, drive growth and increase margin expansion
- To retain high potential individuals
- To attract top new talent
- To be recognized as a center of excellence that focuses on associate learning and growth as a building block for innovation

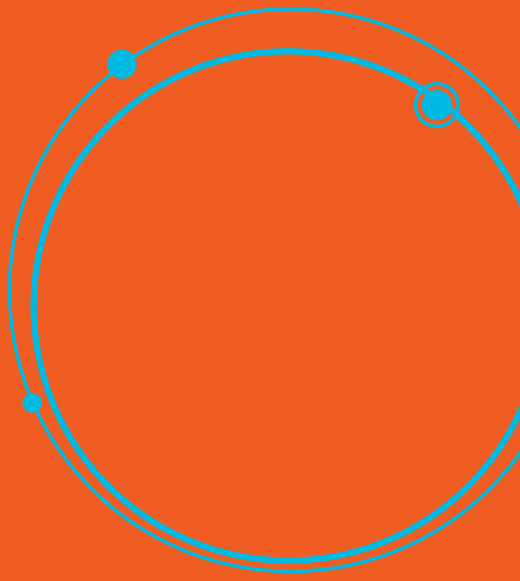
The aim of our operations is to deliver on our core values, developing our pool of talent to drive breakthrough results and achieve excellence in quality, cycle time, and total cost. In 2018, the team introduced a new initiative into our operations processes, using innovation and resources to help us work smarter and create more value, while enhancing our productivity and eliminating waste (Muda). Smart Operations will marry DBS principles with new technological tools – like information systems, cloud computing, autonomation, IoT and additive manufacturing – to help increase productivity.

Our associates are able:

- To belong, be part of the brand, and take pride in being part of a leading organization
- To embark on the journey to be the best, as we encourage learning, development and career progression
- To be empowered and have a sense of ability to make a difference, for themselves, for SCIEX, and for their customers, family and friends

Through challenging and meaningful work, associates develop practical work experience, collaborate with like-minded team mates, and grow professionally. In doing so, we hope to create an engaging organization where associates are proud of their workplace and have a sense of pride in enabling SCIEX to deliver superior products and services of value to customers, have the ability to adapt to changes in the external business environment, and engage in an inclusive environment that values the quality of work life.

BEST TEAM WINS!



Answers for Science.
Knowledge for Life.™

WHATEVER YOUR APPLICATION, THERE'S A SCIEX SOLUTION TO SUIT...

SCIEX M5 and OptiFlow™ Turbo V Source

The feature rich M5 MicroLC microflow chromatography system combines sensitivity, versatility and robustness, simplifying small and large molecule quantitation and characterization while reducing costs, footprint and sample size. The system offers greater sensitivity than traditional analytical flow LC and is more robust than nanoflow LC, and can be easily integrated with a range of SCIEX MS platforms to provide a fully optimized workflow. In addition, the M5 MicroLC is designed to work with any columns and chemicals, and set-up is tool-free, giving you the flexibility and ease to alter configurations for any challenge, to take on any workflow any day.

The M5 MicroLC can be used in combination with the OptiFlow Turbo V source to create the OptiFlow Quant Solution, opening up new possibilities for microflow separation. This solution combines ease of use and robustness of analytical flow with the sensitivity of microflow separation, helping to quantify challenging analytes while maximizing throughput and uptime. It offers flow rates as low as 1 µl/min to boost signals, and up to five-fold improvements in the signal-to-noise ratio for maximum performance and consistent results.

For more information, visit
www.sciex.com/products/integrated-solutions/optiflow-quant-solution

SCIEX X500 series

The X-series QTOF systems are revolutionary for increasing productivity in high throughput analytical labs. The compact design and intuitive user interface of the systems is combined with streamlined data acquisition and analysis capabilities – without compromising power or resolution. These highly powerful benchtop platforms make screening easier and more accurate than ever.

The X500R is the first high resolution system designed for high throughput screening for unknown compounds in food, environmental and forensic testing labs. Its user-friendly workflows, robust hardware and end-to-end balanced performance help ensure seamless implementation and reliable results, making the X500R perfect for routine screening.

The X500B delivers the resolution, robustness and reliability needed to boost analytical capacity for biologics characterization. Its intuitive software and straightforward workflows accelerate throughput, while its compact design takes up the least lab space of any high resolution MS system on the market.

For more information, visit
www.sciex.com/x-series-qtof-systems

SCIEX OS Software

SCIEX OS is the only software solution that combines comprehensive qualitative and quantitative data analysis, improving the productivity of data acquisition and processing. The intuitive user interface – with multiple categorization and filtering options – simplifies data analysis, making data processing faster and easier. New algorithms provide automated integration, outlier removal and native standard addition capabilities, reducing manual interpretation and improving accuracy and reproducibility. Additionally, flexible security features offer the ability to tailor security configurations to meet your needs and help ensure regulatory compliance.

SCIEX OS is the control system for the SCIEX X-series QTOF MS Systems, simplifying the data workflow, and can also be used to analyze data acquired from other SCIEX systems, including the SCIEX Triple Quad™, QTRAP®, and TripleTOF® platforms.

For more information, visit
www.sciex.com/products/software/sciex-os-software

I LOVE MASS SPEC

We have loved receiving all of your entries for this year's 'I love mass spec' feature. At SCIEX, we recognize that mass spectrometry is making a real difference in a variety of scientific sectors, and that is why we continue to develop new innovative products every day. We challenged you to send in a photo that captures the spirit of SCIEX in your lab and show how much you love your mass spec system – here are some of our favorite and most creative entries:

We really enjoyed looking through all of your photos, so don't forget to continue to show us how much you love your mass spec by submitting yours to **vision@sciex.com.**

For all the latest news and views from SCIEX, follow **@SCIEXnews** on Twitter.

By sending us photos, you acknowledge and agree that SCIEX shall have a non-exclusive right to use your images in the SCIEX Journal and other communication materials, in perpetuity, on a worldwide basis without any compensation and without further notice.

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UPCOMING EVENTS

DON'T MISS SCIEX'S EVENTS IN 2019

NORTH AMERICA & CANADA

Emerald Conference
San Diego, CA, USA
27.02-01.03

ASMS 2019
Atlanta, GA, USA
02.06-06.06

AACC 2019
Anaheim, CA, USA
04.08-08.08

SOFT 2019
San Antonio, TX, USA
13.10-18.10

EMEA

World ADC
London, United Kingdom
04.03-06.03

Proteomic Forum 2019 – XIII. Annual Congress of the European Proteomics Association
Potsdam, Germany
24.03-28.03

8th Berliner LC-MS/MS Symposium 2019
Berlin, Germany
02.04

TIAFT
Birmingham,
United Kingdom
02.09-06.09

RAFA
Prague, Czech Republic
05.11-08.11

JAPAN

JASIS Kansai 2019
Osaka, Japan
05.02-07.02

JASIS 2019
Chiba, Japan
04.09-07.09

CHINA

The 2nd CIIE
Shanghai, China
05.11-10.11

AUSTRALIA & SINGAPORE

6th Annual Biologics Manufacturing Asia
Singapore
26.02-28.02

HUPO 2019
Adelaide, Australia
15.09-18.09

SCIEX helps to improve the world we live in by enabling scientists and laboratory analysts to find answers to the complex analytical challenges they face. The company's global leadership and world-class service and support in the capillary electrophoresis and liquid chromatography-mass spectrometry industry have made it a trusted partner to thousands of the scientists and lab analysts worldwide who are focused on basic research, drug discovery and development, food and environmental testing, forensics and clinical research.

With over 40 years of proven innovation, SCIEX excels by listening to and understanding the ever-evolving needs of its customers to develop reliable, sensitive and intuitive solutions that continue to redefine what is achievable in routine and complex analysis. For more information, please visit sciex.com.

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