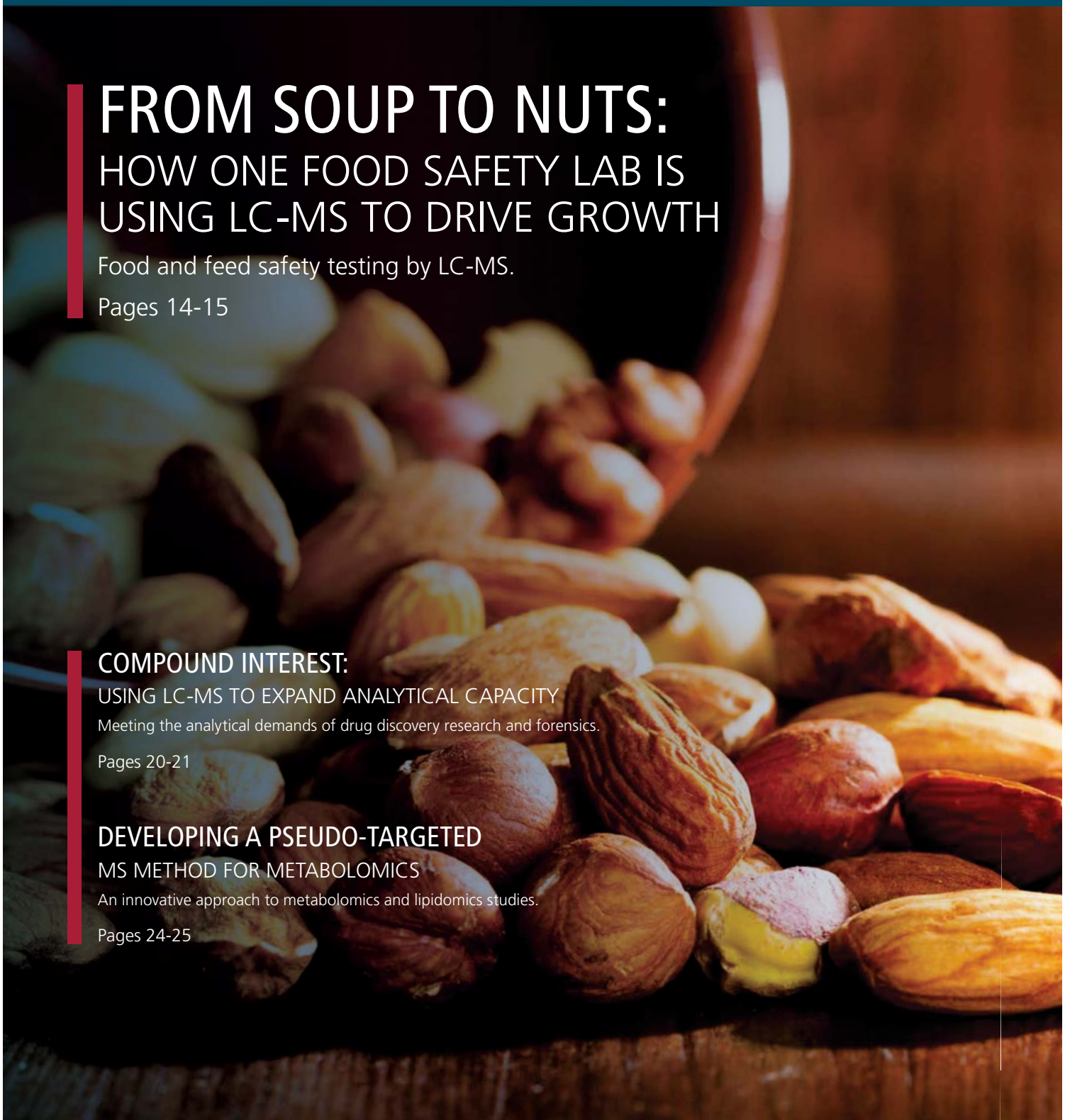
SCIEX | VISION

Issue **3**



# FROM SOUP TO NUTS:
## HOW ONE FOOD SAFETY LAB IS USING LC-MS TO DRIVE GROWTH

Food and feed safety testing by LC-MS.

Pages 14-15

## COMPOUND INTEREST:
### USING LC-MS TO EXPAND ANALYTICAL CAPACITY

Meeting the analytical demands of drug discovery research and forensics.

Pages 20-21

## DEVELOPING A PSEUDO-TARGETED
### MS METHOD FOR METABOLOMICS

An innovative approach to metabolomics and lipidomics studies.

Pages 24-25

# 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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# CONTENTS

# 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**