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MSACL 2015 EU: *Preliminary* Conference Program

Salzburg Congress Center, AUSTRIA • September 8-11, 2015

With Thanks to Our Corporate Sponsors:

**TUESDAY**

9:00 AM
WELCOME COFFEE
@ Mozart 1-3

Enjoy coffee, a muffin and a chat with colleagues before the day starts.

10:00 AM
SHORT COURSES: SESSION 1

*Getting Started with Quantitative LC-MS/MS in the Diagnostic Laboratory*
Judy Stone, PhD & Grace van der Gugten
Level: 1-2 (Beginner - Intermediate)
Location: Mozart 4

*Breaking up with Excel: A Newbie’s Introduction to the R Statistical Programming Language*
Daniel Holmes, MD & Stephen Master, MD PhD
Level: 1-2 (Beginner - Intermediate)
Location: Mozart 5

*Practical LC-MS Maintenance and Troubleshooting (Tuesday)*
Erik J. Soderblom, PhD, Christopher Shuford, PhD, J. Will Thompson, PhD
Level: 2 (Intermediate)
Location: Trakl Hall
Registration for either day of this course (Tuesday or Wednesday) allows you to attend both days.

*Development and Validation of Quantitative LC-MS/MS Assays for Use in Clinical Diagnostics*
Russell Grant, PhD & Brian Rappold
Level: 3 (Advanced)
Location: Papageno Hall
LUNCH
@ Mozart 1-3
Lunch to be provided in Mozart 1-3 with the possibility to eat outside in front of the Congress Center on bistro tables, weather permitting.

SHORT COURSES: SESSION 2

COFFEE BREAK
@ Mozart 1-3
Take a break and get a coffee, water and/or snack. Commune with colleagues or perhaps go for a short walk outside to refresh for the next session.

SHORT COURSES: SESSION 3

WORKING DINNER
@ Mozart 1-3
An evening buffet working dinner with appetizers and drinks to allow you time to connect with your instructor and classmates before the last hour of class for the day!

SHORT COURSES: SESSION 4

ENJOY THE CITY
@ Salzburg Old City
Explore the Old Town of Salzburg.

TUESDAY CLOSED

WEDNESDAY

WELCOME COFFEE
@ Mozart 1-3
Enjoy coffee, a muffin and a chat with colleagues before the day starts.

SHORT COURSES: SESSION 1

Getting Started with Quantitative LC-MS/MS in the Diagnostic Laboratory
Continued from Saturday
Judy Stone, PhD & Grace van der Gugten
Level: 1-2 (Beginner - Intermediate)
Location: Mozart 4

Breaking up with Excel: A Newbie's Introduction to the R Statistical Programming Language
Continued from Saturday
Daniel Holmes, MD & Stephen Master, MD PhD
Level: 1-2 (Beginner - Intermediate)
Location: Mozart 5

Detection Of Pathogens By Whole-Cell MALDI-TOF MS And Advanced Proteomics Approaches
Jean-Armengaud, PhD, Oliver Pible & Julia Chamot-Rooke, PhD
Level: 1-2 (Beginner - Intermediate)
Location: Paracelsus Hall

Practical LC-MS Maintenance and Troubleshooting (Wednesday)
Erik J. Soderblom, PhD, Christopher Shuford, PhD, J. Will Thompson, PhD
Level: 2 (Intermediate)
Location: Trakl Hall
Registration for either day of this course (Tuesday or Wednesday) allows you to attend both days.

Development and Validation of Quantitative LC-MS/MS Assays for Use in Clinical Diagnostics
Continued from Saturday
Russell Grant, PhD & Brian Rappold
Level: 3 (Advanced)
Location: Papageno Hall

**COFFEE BREAK**
* @ Mozart 1-3

Take a break and get a coffee, water and/or snack. Commune with colleagues or perhaps go for a short walk outside to refresh for the next session.

**SHORT COURSES: SESSION 2**

**LUNCH**
* @ Mozart 1-3

Lunch to be provided in Mozart 1-3 with the possibility to eat outside in front of the Congress Center on bistro tables, weather permitting.

Fresh air has been reported to assist in reduced lethargy and increased levels of Vitamin D (if accompanied by sun exposure).

**SHORT COURSES: SESSION 3**

**COFFEE BREAK**
* @ Mozart 1-3

Take a break and get a coffee, water and/or snack. Commune with colleagues or perhaps go for a short walk outside to refresh for the next session. POSTER PRESENTERS: If you are presenting a poster today, it should be placed by the end of this break.

**SHORT COURSES: SESSION 4**

**OPENING RECEPTION**
* @ Exhibit Hall / 1st Floor

Enjoy mingling with colleagues and Exhibitors. Take time to explore the Posters, which will be attended from 6:00 - 7:00 PM. Buffet dinner and drinks to be provided.

**POSTERS**
* @ Exhibit Hall / 1st Floor

ALL Posters Attended from 6:00 - 7:00 PM.

**ENJOY THE CITY**
* @ Salzburg Old City

Explore the Old Town of Salzburg.

**WEDNESDAY CLOSED**

**THURSDAY**

**PLACE POSTERS**
* @ Exhibit Hall / 1st Floor

Poster presenters for Thursday must have their posters placed by 9 AM.

**WELCOME COFFEE**
* @ Registration Foyer

Enjoy coffee, a muffin and a chat with colleagues before the day starts.

**CORPORATE WORKSHOPS (8:00 - 8:40 AM)**

*Thermo Scientific*
Papageno Hall
Pre-Register

Discover four medical devices for general clinical use: Thermo Scientific™ Prelude MD™ HPLC, Thermo Scientific™ Prelude LX-4 MD™ HPLC, Thermo Scientific™ Endura MD™ mass spectrometer, and Thermo Scientific™ ClinQuan MD™ Software. Clinical laboratories can use these devices to build their own lab developed tests (LDT). Various example compounds and workflows will be used to demonstrate the robustness and time efficiency of these new medical devices. For in vitro diagnostic use. Not available in all countries.

WELCOME, INTRODUCTION & ORIENTATION
@ Mozart Hall

Welcome to the 2nd Annual European MSACL Congress!

Congress Mobile Apps
Two apps to facilitate contact collection and Scientific Program browsing.

8:45 AM

(1) The Mobile Program App
Online @ https://www.msacl.org/mobile

(2) BadgerScan™ for Contact Lead Collection.
Available on Google Play and the Apple App Store (iTunes).

PLENARY LECTURE SERIES
@ Mozart Hall
Chair: Michael Vogeser & Oleg Mayboroda

9:00 AM
9:45 AM

Mass Spectrometry as Metrological Anchor in Laboratory Medicine – a Meandering River
Linda MR Thienpont
Ghent University
Long Abstract | Biography | Financial Disclosure

Distinguished Contribution Awardee
The fundament of mass spectrometric (MS) work is the SI base unit “mole”, more in particular, quantitative MS establishes SI-traceability (mol/L) of measurement results. I will discuss the anchors and regulatory surrounding to implement SI-traceability in laboratory medicine. When I entered this field, I thought my scientific life would be a “fast-flowing river”. However, several obstacles forced it to meander, e.g., concepts like biological variation, analytical performance goals, commutability, and the introduction of MS in routine. Although I tried to cope with these obstacles, “my river” continues to meander. As an outlook, I will present some of my most recent work.

9:45 AM
10:30 AM

The Cellular Uptake of Pharmaceutical Drugs Is Transporter-Mediated and Is Thus a Problem Not of Biophysics But of Systems Biology
Douglas Kell
The University of Manchester

A fundamental question remains as to whether xenobiotic drugs cross cellular membranes mainly (or exclusively) by transporter-independent diffusion across whatever bilayer lipoidal parts of cellular membranes may be present, or whether they normally (or exclusively) ‘hitchhike’ rides using the carriers normally involved in the metabolism of natural metabolites. The former (for which, astonishingly, there is in fact no actual experimental evidence) would involve a biophysical mechanism, based mainly on lipophilicity, while the latter requires a mechanistic understanding of which carriers are involved, and is thus a problem of network or systems biology. In other words, “is carrier-mediated transport of pharmaceutical drugs the exception or the rule?” A huge amount of literature (see Long Abstract), that I shall summarise, indicates that there is no serious evidence
against the view that trans-phospholayer-mediated transfer of pharmaceutical drugs across biological membranes is negligible (‘PBIN’), while there is abundant and increasing evidence for the carrier-mediated route. A recent approach in yeast illustrates this experimentally, while the digital availability of principled metabolic network models allows one to determine, consistent with this, that successful pharmaceutical drugs are much more like metabolites than are the ‘Lipinski-compliant’ molecules typically available in drug discovery libraries. This suggests (or is at least consistent with the view) that cellular drug uptake is more or less exclusively transporter-mediated, and that knowledge of both the metabolome and of the concentrations and activities of transporters used by individual xenobiotics will be of much value in designing better drugs and bioprocesses.

COFFEE BREAK
@ Exhibit Hall / 1st Floor
Visit the Exhibit Hall to procure coffee, juice, water and/or snacks. Explore what's on offer from the Exhibiting vendors, reconnect with colleagues, or go for a short walk outside to refresh for the next session. POSTER PRESENTERS: If you are presenting a poster today your poster should have been up 2 hours ago. If it is not up please put it up immediately.

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GENERAL SCIENTIFIC SESSION 1

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<td>Proteomics Assay Development</td>
<td>Paracelsus Hall</td>
<td>Intro to Mass Spec</td>
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<td>Chair: Jody van den Ouweland</td>
<td>Chair: Uta Ceglarek</td>
<td>Chair: Steve Master</td>
<td>Chair: David Phelps</td>
<td>Chair: Jane Yang</td>
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11:15 AM 11:40 AM

**Design of Optimization: How to Systematically Improve the Performance of High Volume LC-MS/MS Clinical Assays**

Brian Rappold

*Essential Testing Long Abstract*

Method optimization is largely a colloquial term for LC/MS/MS users. The extent of optimization can range from cursory evaluations during core development experiments to substantive investigations of all variables associated with a method. Unlike design of experimentation which requires broad assumptions and large experimental parameter shifts, design of optimization relies on efficiently designed experimentation with the ability to produce dramatic improvement of the time that ovarian, shown for the first time that ovarian, survival is 43.5%.

Ovarian cancer is common and 5-year survival is 43.5%. Surgeons use intra-operative frozen section for tissue identification but this is time-consuming and expensive. Microscopic non-descript lesions during surgery, which may be cancer can be difficult to correctly identify. The near-real-time tissue identification abilities of the iKnife were tested in this study. We have shown for the first time that ovarian,
valid conclusions. This paper will introduce a practical series of experimental frameworks to scientifically rationalize the parameters and processes involved in optimization of a clinical diagnostics assay. Examples will be shown from assays which analyze more than 500 specimen/day.

multiplexing, which was collectively demonstrated in numerous pilot studies worldwide. Besides the latest development and clinical data from pilot studies, we are planning to present on the absolute enzyme activity measurement in highly purified leukocyte populations as a second-tier diagnostic test, which is transforming the field.

reliability and the precision of the analyses. The method has a broad applicability to the quantitative analysis of clinical samples, such as lung cancer plasma samples to discriminate the disease stages and subtypes; and to tissue samples to map driver mutations (EGFR and KRAS).

peritoneal and fallopian tube tissues have unique REIMS spectral signatures, which can be used to accurately classify tissue histopathology. Leave-one out patient cross-validation resulted in 100% sensitivity and 100% specificity in the separation of normal and cancerous ovary (n=189).

| 11:40 AM | What Is Wrong in Your LC-MS Analysis? Post Column Infusion as a Diagnosis Tool |
| 12:05 PM | Oskar Gonzalez |

Oskar Gonzalez | University of the Basque Country |

**Long Abstract** | Bio

Continuous post-column infusion of standards is a very useful tool to obtain additional and very valuable information about a LC-MS method. Here we show multiple applications of this technique in method development and routine analysis based on our experience in the laboratory: detection of compounds causing ion suppression, aid in sample treatment choice, understanding of abnormal results, compensation of matrix effect and some others.

Considering all these benefits, we encourage to use this technique in clinical analysis to improve the reliability of LC-MS methods and to obtain more accurate results.

Research into Lysosomal Storage Metabolism Using Plasma Lipid Characterization by LC-MS/MS

Dan Blake | SCIEX

**Long Abstract** | Bio | Financial Disclosure

Research into plasma sphingolipids and determining the concentrations of such is of growing importance in the clinical research laboratory, particularly within groups researching Lysosomal Storage Metabolism. Current methods of analysis primarily involve either enzyme activity procedures or derivatization of compounds prior to analysis. Direct analysis of these groups can be complex due to extensive structural homogeneity between individual compounds. We present here a method for a direct multi-compound approach to this analysis, employing modern advances in column technology to produce a rapid and sensitive LC-MS/MS method for these compounds.

MS-based Serum Proteomics in Clinical Chemistry: Requirements for Candidate Translation and Implementation as a Routine Assay

Christa Cobbaert | Leiden University Medical Center

**Long Abstract**

Numerous serum protein profiling efforts have aimed for biomarker discovery since the early days of mass spectrometry(MS)-based proteomics. These pipelines have yielded many promising protein candidates, but disappointingly none of these has been translated into a truly validated medical test. Alternatively, strategies have been followed to convert existing routine uniplex protein assays into an MS-based in-vitro diagnostic test, however also in this case the success rate has been low so far.

In this presentation both approaches will be discussed with regard to requirements needed for translation or implementation these into a clinical chemistry laboratory.

The Mucosal Metabolome: Real-time Rapid Medical Swab Point-of-care Analysis Using TFME-DESI MS to Reveal Pathogenic and Inflammatory Metabolomic Markers

Pamela Pruski | Imperial College London

**Long Abstract** | Bio

The mucosal membrane, a protective layer responsible for trapping pathogens in the human body, is an easily accessible and highly clinically relevant sample to diagnose pathogenic and cancerous associated diseases. Since DESI MS is not applicable for in-vivo analysis due to the potential risk of electrical shock and the use of organic solvent, medical swabs are a standard collection device for mucosal membranes that can be directly analysed with DESI MS. Chemical signatures identification of specific bacteria within minutes on the surface of swabs would provide a rapid diagnosis of infections associated

Introduction to Ionization Modes in Mass Spectrometry

Jörg Hanrieder | University of Gothenburg

**Long Abstract**

Ionization of analytes into the gas phase is a critical step for accurate mass identification. Various types of ionization methods can be applied for optimal analyte identification. This session will involve a basic introduction to various ionization modes used in mass spectrometry and will discuss the advantages and disadvantages of each.
Fully Automated Multi-Method LC-MS: Application in Clinical Laboratory
Marco Cantù
Ente Ospedaliero Cantonale

Long Abstract | Bio
In the last 4 years we setup a flexible configuration able to do different analytical methods on a single LCMS. This configuration is able to load simultaneously: up to 24 solvents into the primary pump, up to 4 solvents into the secondary pump, up to 15 columns, divided into 2 independent thermostats. This system is able to manage all instrument’s changes (solvent line selection, column selection, etc.) directly from the work-list. This is a real huge result that open the possibility to process urgent samples just adding them into the work-list also while the LCMS is processing other methods, without any switch off, changes and restart.

Preeclampsia Risk Stratification Early in Pregnancy: First Results of a New LC-MS Based Multiplex Metabolite Assay
Robin Tuytten
Metabolomic Diagnostics

Long Abstract | Bio | Financial Disclosure
Preeclampsia is one of the major complications of pregnancy. First time pregnant women have an increased risk for preeclampsia, yet routine prenatal care fails to accurately identify the 1st time pregnant women at risk. Basic biomarker research revealed that blood borne metabolites bear potential to risk-stratif for preeclampsia early in pregnancy. In a dedicated translational research effort, a prototype multiplex metabolite LC-MS assay was developed and then applied to a large case:control study focusing on 1st time pregnant women. This study confirmed that the newly discovered metabolite biomarkers enable prediction of preeclampsia risk early in pregnancy.

The Holy Trinity: The Inter-relationship of Standards, Matrix, and Internal Standardization in Protein Cleavage Isotope Dilution Mass Spectrometry (PC-IDMS)
Russell Grant
Laboratory Corporation of America

Long Abstract | Bio | Financial Disclosure
To better understand the inter-relationship of calibration (matrix and standard) and internal standardization on the accuracy of digestion-based protein quantification, the relative digestion efficiency of multiple internal standard types (peptides/protein), multiple standardized forms of unlabeled protein (recombinant/human-derived) and multiple matrices (true/surrogate) are evaluated for quantifying thyroglobulin in serum using multiple signature peptides. Comparing multiple matrices and protein standards will differentiate if the disparities/similarities between peptides are matrix effects and/or specific to the analytical standard used. A variety of digestion conditions are explored in combination with different internal standards to determine if disparities between peptides can be validated on each?

DESI-MS and REIMS as Excellent Techniques to Complement and Support Histology in Ovarian Cancer
Luisa Doria
Imperial College of London

Long Abstract | Bio
Ovarian cancer is the fifth most common cancer among women and one of the causes is the poor and vague prognosis and diagnosis. REIMS and DESI-MS are two mass spectrometry techniques with great potential to characterise and discriminate different cancer types and stages. Both techniques are excellent to complement and support histology, REIMS can identify different ovarian cancer types in real time and DESI can provide detailed spatial information within the sample giving the opportunity to investigate tumour biology from an entirely new perspective with accurate biochemical information about each tissue type.

Introduction to Mass Analyzers: Quadrupole vs. Time-Of-Flight (TOF)
Jörg Hanrieder

Young Investigator Grant
University of Gothenburg

Long Abstract
Choosing a mass analyzer for clinical analysis is an important step in setting up a mass spectrometry laboratory. But what is a mass analyzer? Are all mass analyzers are created equal? What types of clinical tests can be validated on each? Each type of mass analyzer has its own benefits and caveats in mass resolution, sensitivity, and dynamic range for small molecule analysis. Choosing a mass analyzer to suit the needs of the clinical laboratory is an important consideration to make. This lecture will focus on quadrupole and time of flight (TOF) mass analyzers for identification and quantification of small molecules. This lecture will also describe how these different mass analyzers actually create mass separations and will describe the various clinical applications available to each.
mitigated.

**LUNCH**
@ Exhibit Hall / 1st Floor
Lunch to be provided in the Exhibit Hall. • Get ready to join a Corporate Workshop after the poster session.

**POSTERS**
@ Exhibit Hall / 1st Floor
All Posters to be attended from 1:30 - 2:30 PM.

**CORPORATE WORKSHOPS (2:30 - 3:30 PM)**

**Shimadzu**
Mozart 1-3
Smart Solutions: Fully Automated Systems for Your Laboratory
Applications
Pre-Register
1. TDMPREP - Centrifugation Free Sample Preparation with Magnetic Beads!
Mario WUTTKE, Magnamedics, Netherlands
2. New Developments in NBS using DBS for Metabolic Profiling including Steroids
Prof David C. KASPER, MedUni Vienna/ARCHIMEDlife, Austria
3. New LCMS-8060: Opens Up the Way for New Applications
Stephane MOREAU, Shimadzu Europa Gmbh, Germany
4. Fully Automated System including Sample Preparation
Stephane MOREAU, Shimadzu Europa Gmbh, Germany

**Thermo Scientific**
Mozart 4-5
Identifying Unknown Unknowns with High Resolution Accurate Mass MS in Toxicology
Robert Mistrik, HighChem Pre-Register

**Agilent Technologies**
Workshops on StreamSelect, Metabolic Workflows and Sample Prep with AssayMAP Bravo
1. Introducing the New Agilent StreamSelect LC/MS System
Pete Christensen, PhD, Agilent Technologies, UK
2. Metabolomic Workflows for Clinical Research-demonstrating a tool to address investigation of inborn metabolic errors
Dr. Holger Stalz, Agilent Technologies, Switzerland
3. Rethink your Protein Sample Preparation Strategy with Agilent AssayMAP Bravo
Moritz Wagner, PhD, Agilent Technologies, Germany

**Spark Holland**
Paracelsus Hall
Scientific and Instrumental Advances in Dried Blood Spot Analysis
Christophe Stove and Bert Ooms
Dried blood spot analysis is emerging as a useful tool for quantitative bioanalysis, particularly for micro volumes of blood or plasma. DBS enables remote sampling in low resource settings or at-home sampling for out-patients. The micro-volume concept helps to reduce lab-animal use and allows use of finger prick instead of venous puncture, making the technique easier applicable for children. However, issues such as the effect of hematocrit on spot size have hindered broad acceptance of DBS for routine bioanalysis. Recent innovations have addressed these issues and will be presented and discussed in this workshop by professor Christophe Stove (Gent University). An introduction to the new DBS autosampler from Spark Holland will be presented by Bert Ooms, principal scientist(Spark Holland).

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@ Exhibit Hall / 1st Floor
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Sponsored by:
For decades immunoassays were applied in an attempt to quantify the cardiac glycoside ouabain in plasma of patients with cardiovascular conditions. This compound (CAS 630-60-4) was supposed to be of endogenous origin as a counterpart of exogenous cardiac glycosides such as digoxin. Using a fully validated, highly specific and extremely sensitive LC-MS/MS method we were able to show that ouabain cannot be present in relevant concentrations in human plasma - as claimed by immunoassay studies.

The quantitative analysis of endogenous steroid hormones cuts across plasma, serum, saliva, urine, dried blood and hair rendering immunological analysis laborious due to the need of different methods. We developed a unifying, highly adaptive LC-MS/MS-method covering the most important endogenous steroid hormones. With excellent interday imprecision (3.15%), very high recovery (89.103%) and a total runtime of 5.0 min we enabled rapid, multi-matrix analysis utilizing MRM and MS² in modified, positive and negative electrospray ionization. Online sample clean-up via automatic column switching combined with an extremely simple dilute-and-shoot sample preparation allows high throughput analysis in clinical routine diagnostics and epidemiological studies.

We report a multiplexed LC-MRM-MS method for the precise quantification of 97 endogenous proteins in human DBS samples, suitable for biomedical research applications. Standard curves were generated for each of the 173 target peptides (representing the 97 proteins) to fully characterize the assay’s analytical merits. Furthermore, the stability of each target peptide was investigated in DBS samples stored at -20°C, 4°C, RT and 37°C over a duration of 154 days. Finally, we will present a simple strategy for managing the hematocrit effect across samples and discuss the implications on the DBS-MRM workflow.

For decades immunoassays were applied in an attempt to quantify the cardiac glycoside ouabain in plasma of patients with cardiovascular conditions. This compound (CAS 630-60-4) was supposed to be of endogenous origin as a counterpart of exogenous cardiac glycosides such as digoxin. Using a fully validated, highly specific and extremely sensitive LC-MS/MS method we were able to show that ouabain cannot be present in relevant concentrations in human plasma - as claimed by immunoassay studies.
Quantitation of Desmosine in Plasma by LC-MS/MS as Biomarkers for Elastin Degradation
Jody van den Ouweland
Canisius-Wilhelmina Hospital

Long Abstract | Bio
Desmosine is a promising biomarker for estimating activity of elastin degradation in patients with COPD, although its clinical validity remains uncertain as reliable and sensitive assays are lacking. An LC-MS/MS method for measuring plasma desmosine was developed and validated. Sample preparation consisted of acid hydrolysis, cellulose SPE using D4-DES as IS, followed by C18 chromatography and MS-analysis using SRM. Measuring range was 0.1-10 ng/ml, imprecision <10%, with recoveries within 80-120%. Plasma desmosine levels from COPD patients were significantly higher compared with healthy individuals. The LC-MS/MS assay appears a valuable tool to assess the potential of desmosine as a biomarker for monitoring disease activity in COPD and to study the effect of therapeutic interventions.

Strategy to Identify and Validate Urinary Steroid Biomarkers Obtained by Untargeted LC-MS/MS Metabolomics: Application to Human Cases of Dioxin Exposure Fabienne Jeanneret
University of Geneva

Long Abstract | Bio
In vitro metabolic reactions were investigated to improve the identification rate from urinary biomarkers obtained by untargeted metabolomic approaches. A previous study performed with UHPLC-QTOF highlighted a subset of 24 urinary steroid and bile acid biomarkers in human cases of acute dioxin exposure. Biosynthesis of glucuronide and sulfate conjugates of biomarker candidates, respectively produced in human liver microsomes and cytosolic fractions, was demonstrated as a successful approach to identify urinary metabolites when authentic chemical standards are not commercially available. Analysis of the biomarkers subset in an independent human cohort exposed to dioxins strengthened the hypothesis of dysregulated profiles of steroids and bile acids.

Quantification of Human Receptor Tyrosine-protein Kinase Erbb-2 (HER2) by Targeted Mass Spectrometry in Formalin-Fixed Paraffin-Embedded Breast Cancer Tissue Axel Ducret
F. Hoffmann-La Roche Ltd

Long Abstract | Bio
We describe in this study a selected reaction monitoring (SRM) assay for the quantification of HER2 in FFPE tissues. The assay's six best candidate peptides showed a linear response over a calibration range of 0.012 to 100 fmol on column (R2: 0.99–1.00) and a lower limit of quantification of 0.155 fmol on column. HER2 peptides were quantified in a cohort of 40 breast tumors expressing different HER2 levels (FISH ratio: 0-2, 2-4, 4-10 and >10 respectively). The SRM assay showed good analytical performance and a high agreement with IHC and FISH data. Furthermore, after normalization for tissue sample size, SRM peptide measurements were able to correctly predict 90% of HER2 amplification status as defined by American Society of Clinical Oncology and College of American

Skin Imprinting in Silica Plates: A Potential Diagnostic Methodology for Leprosy Using High-Resolution Mass Spectrometry
Estela de Oliveira Lima
Universidade Estadual de Campinas

Long Abstract | Bio
Leprosy is an infectious disease caused by Mycobacterium leprae, primarily present at skin macrophages and Schwann cells. Presently, the available laboratorial diagnostic methods for leprosy are invasive, expensive, and present low sensibility for the asymptomatic cases. Therefore, this work intended to develop a noninvasive, fast and sensible method for leprosy diagnosis, associated to high-resolution mass spectrometry. Our data analysis has elected two mycobacterial biomarkers at leprosy skin patients, absent at control samples. These results indicate that our new methodology can be candidate as a fast and sensible leprosy diagnostic method, even for patients without clinical skin manifestations.

Varying Those Vexing Voltages: Compound Specific Tuning
Daniel Holmes
St. Paul's Hospital, Vancouver

After ensuring your instrument’s resolution and mass accuracy are appropriately set, the next step in developing a quantitative LC-MS/MS multiple reaction monitoring (MRM) assay is to perform compound-specific tuning. Well-defined signal-optimization experiments are used to determine appropriate ion source electronics and gas flow parameters to specifically quantify the compound of interest. This overview will introduce basic concepts of so-called "compound optimization". In other words, we will explain what is meant when people say that they have "developed mass spectrometric method."
**Assaying Protein Unbound Drugs Using a Highly Sensitive LC-MS/MS Method**

Heike Bittersohl

*Long Abstract* | Bio
Therapeutic monitoring of protein unbound (free) immunosuppressants has the potential to better predict the clinical outcome compared to conventional monitoring of drug levels in whole blood or plasma. Only a small proportion of drugs are free in the patient blood, hence, requiring a sensitive analytical method for their determination. We established an LC-MS/MS method able to simultaneously measure levels of cyclosporine A and mycophenolic acid in the picomolar range. This procedure is currently applied in a study on samples from kidney transplant recipients taking both drugs as a combination therapy.

**Not Always CAH. Urine Steroid Profiling in the Investigation and Diagnosis of Adrenal Causes of Neonatal Hypoponatraemia and Failure to Thrive**

Francis Lam

*Long Abstract* | Bio
A baby presented at a local hospital with failure to thrive. Initial biochemistry showed hyponatraemia and hyperkalaemia. Other blood analyses were inconclusive. A spot urine sample was sent for urine steroid profile (USP) analysis. The USP showed a relative abundance of corticosterone metabolites with undetectable tetrahydroaldosterone, a pattern indicative of aldosterone synthase deficiency, subsequently confirmed by genetic testing in this laboratory. Where a steroid disorder is suspected, a USP has great utility since the specimen is easily accessible and can identify/exclude a variety of disorders. Where urgent samples are involved, analyses can be prioritised with relatively rapid turnaround time.

**Calculated HbA1c from Total Glycated Hemoglobin by Quantitative MALDI-TOF Mass Spectrometry**

Jane Yang

*UCSD Long Abstract* | Financial Disclosure
Percent HbA1c, the standard measure of glycated hemoglobin used to diagnose and monitor diabetes mellitus, correlates linearly with total glycated hemoglobin (tGHb). MALDI-TOF mass spectrometry of whole blood hemolysates allows the direct quantitation of the total glycated hemoglobin (tGHb) ratios of alpha and beta chains from a single mass spectrum. Sample preparation for this approach is minimal, analysis is rapid, 80 spots in 20 min (15 sec/spot), and hemoglobin variants are also detected. tGHb by MALDI is reproducible with intra-plate CVs < 1.4%, linear vs. cation exchange HPLC (y = 1.20x – 1.07; R² = 0.99) from 2.7% to 22% A1c. MALDI method is faster and less expensive than HPLC.

**Discrimination and Relative Quantitation of Closely Related Pathogens in Complex Clinical Samples**

Olivier Pible

*CEA Long Abstract* | Bio
Mass spectrometry is a powerful tool to identify pathogens. However some issues such as mixture handling are usually beyond reach of whole-cell MALDI-TOF approaches. We developed a tandem mass spectrometry approach which not only can address complicated samples such as mixtures of any organisms, but can also give access to relative quantitation of pathogens. It is based on the analysis of the peptide content of the sample and the extraction of phylogenetic information. An universal organism signature has been characterized using this molecular information. The identification problem is then reduced to the search of the linear combination of organism signatures which best matches the overall mass spectrometry signal.

**Building your Assay, Breaking your Compound: Developing MRM Transitions**

Stephen Master

*Weill Cornell Medical College Long Abstract* | Bio
Now that you know how to perform compound-specific tuning, you are ready to build your assay. In this session, we will explore how to take a compound that you're interested in measuring by mass spectrometry, break it apart, and pick appropriate product ions for quantitation. This is the final step that allows you to sensitively and specifically measure the abundance of your desired analyte.

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**RECEPTION**

@ Exhibit Hall / 1st Floor

Enjoy mingling with colleagues and Exhibitors. Take time to browse the posters. Buffet dinner, appetizers and drinks to be provided. POSTER PRESENTERS: Remove posters between 7:30 - 7:45 PM.

*Sponsored by:*

[Thermo Scientific](https://www.thermo.com)

**PLENARY LECTURE SERIES**

@ Mozart Hall

*Chair: Russell Grant*
Why Patients Adore Mass Spectrometry
Andy Hoofnagle
University of Washington

Physicians rely on high quality measurements of small molecules and proteins for the diagnosis, prognosis, and management of disease. Health care providers have become reliant on relatively inexpensive, high-throughput immunoassays to capture biomarker data from patient samples. Unfortunately, these assays can be misleading. Clinical mass spectrometric assays bring sensitivity and specificity together in previously unthinkable ways and span the range of medical specialties. This talk will describe the ways in which mass spectrometry can improve the care of our patients.

FRIDAY

PLACE POSTERS
@ Exhibit Hall / 1st Floor
Poster presenters for Friday must have their posters placed by 9 AM.

WELCOME COFFEE
@ Registration Foyer
Enjoy coffee, a muffin and a chat with colleagues before the day starts.

PLENARY LECTURE SERIES
@ Mozart Hall
Chair: TBA

Steroid Metabolomics as a Discovery Tool
Wiebke Arlt
Institute of Metabolism & Systems Research, University of Birmingham, UK

Our group employs steroid metabolomics to reveal the pathogenesis and identify diagnostic and prognostic biomarkers in steroid-producing and steroid-dependent disease. Our approach uses gas chromatography - mass spectrometry (GC-MS) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) coupled with computational data analysis by machine learning-based approaches. I will present a number of examples including adrenal disorders, hypertension and steroid-dependent cancer to illustrate the power of this approach.

Innovative Instrumentation and Methods for the Identification of Intact Proteins in Mixtures and for Sequence Analysis of Antibodies and Posttranslationally-Modified, Intact Proteins on a Chromatographic Time-Scale
Donald Hunt
University of Virginia

This lecture will focus on data generated with a new ion source that facilitates simultaneous generation of positively charged sample ions by electrospray ionization and negatively charged reagent ions for both electron transfer dissociation (ETD) and ion-ion proton transfer (IIPT) reactions on Orbitrap mass spectrometers. Implementation of multiple C-trap fills for enhanced sensitivity will be discussed and both parallel peak parking, and ion ejection strategies to facilitate protein separation and enhanced sequence coverage of intact proteins will be described. Use of IIPT/ETD facilitates near complete sequence coverage on many intact proteins and is ideally suited for locating multiple posttranslational modifications on the same protein molecule. Sequence analysis of antibodies with an enzyme reactor that generates 3-10 KDa fragments in seconds will also be discussed. If time permits, the lecture will also provide an update on the use Class I MHC phosphopeptides for the immunotherapy of cancer.

COFFEE BREAK
@ Exhibit Hall / 1st Floor
Visit the Exhibit Hall to procure coffee, juice, water and/or snacks. Explore what's on offer from the Exhibiting vendors, reconnect with colleagues, or go for a short walk outside to refresh for the next session. POSTER PRESENTERS: If you are presenting a poster today your poster should have been up 2 hours ago. If it is not up please put it up immediately.
Ferromagnetic Particles as a Rapid and Robust Sample Preparation for Absolute Quantification of Eicosanoids

Anna Catharina Suhr
Young Investigator Grant
Laboratory Medicine, Munich (LMU)

Long Abstract | Bio

We used ferromagnetic particles as a novel technique to deproteinize plasma samples prior to UHPLC-MS/MS analysis for the quantification of important lipid mediators. A combination of "ferromagnetic particle enhanced deproteinization" and subsequent "on-line solid phase extraction" realises quick and convenient sample preparation as well as it provides high sensitivity and robustness. We were able to show that this approach allows accurate and precise quantification of seven exemplary eicosanoids (TXB2, PGE2, PGD2, 5-HETE, 11-HETE, 12-HETE, and arachidonic acid). The use of this semi-automated sample preparation facilitates the screening of large samples prior to UHPLC-MS/MS analysis.

Development of Quantitative UPLC-MS/MS Method for Clinical Diagnosis of Rare Kidney Stones and Kidney Failure

Finnur Eiriksson
University of Iceland

Long Abstract | Bio

Adenine phosphoribosyltransferase (APRT) deficiency results in excessive urinary excretion of poorly soluble 2,8-dihydroxyadenine (DHA) causing kidney disease. Treatment with allopurinol and febuxostat prevents the disease in patients with APRT deficiency. Therapeutic drug monitoring is currently performed by urine microscopy but a more sensitive and reliable method is needed. A UPLC-MS/MS method was developed and utilized to measure the concentration of DHA in urine samples from 28 patients, before and after treatment with allopurinol or febuxostat. Significant changes were observed in urinary excretion of DHA after pharmacotherapy was initiated. A decrease in the DHA-to-creatinine ratio was observed with both allopurinol and febuxostat therapy. The developed UPLC-MS/MS assay will greatly facilitate clinical diagnosis and therapeutic drug monitoring in patients with APRT.
Two kinds of solid nanostructure matrices, TiO2 nanowires and functional nanowebbs, were synthesized to detect small molecules from human serum and dairy milk samples by MALDI-TOF MS. TiO2 nanowires were synthesized by top-down hydrothermal process, and functional nanowebbs were synthesized by electrospinning on the metal plate. The feasibility of applying solid nanostructure matrices to MALDI-TOF MS was demonstrated by the detection of short peptides and amino acids. For the real sample analysis, amino acids and antibiotics were spiked into human sera and milk, respectively. The deficiency. From 100 µg to 10 µg. The current lower limit of detection is 0.35 pg Akt1/µg lysate protein. We have developed iMALDI Akt1 and Akt2 assays for quantitation of non-phosphorylated Akt1 and Akt2.

The C-terminal Fragment of Prostate-specific Antigen, a 2331 Da Peptide, as a New Urinary Pathognomonic Biomarker Candidate for Diagnosing Prostate Cancer

Kenji Nakayama Shimadzu Techno-Research (Kyoto Univ. Hospital)

The major pathological hallmarks of Alzheimer’s disease (AD) is the progressive accumulation and aggregation of beta-amyloid (Aβ) and phospho-tau, into neurotoxic deposits. However, the exact molecular processes underlying protein aggregation and plaque pathology remains unknown. The primary goal of this project was to employ advanced molecular imaging mass spectrometry (IMS) to probe the chemical and structural aspects of Aβ plaque pathology in experimental AD. MALDI IMS followed by multivariate image analysis allowed us to avoid the chemical and structural aspects of Aβ plaque pathology in experimental AD.
Development of a UPLC-MS/MS Method to Measure Neurotransmitters and Trace Amines in Human Plasma

Antonina Gucciardi
University of Padova, Italy

Long Abstract | Bio

We developed and validated a method for measurement of plasma neurotransmitters (dopamine, epinephrine, norepinephrine, serotonin) and trace amines (tyramine, octopamine, phenylethylamine, synephrine, β-octopamine, and tryptamine) by UPLC-MS/MS. Analytes were extracted using weak cation exchange SPE and separated by a PFP column and water-acetonitrile-methanol gradient as mobile phase, into the ACQUITY UPLC system. The metabolites were measured in MRM mode with positive electrospray ionization using a NanoElectrospray High Resolution Mass Spectrometry or Liquid Chromatography High Resolution Mass Spectrometry for Urinary Metabolic Profiling?

Elena Chekmeneva
Imperial College London

Long Abstract | Bio

We present a practical comparison of nESI-HRMS and reversed-phase UPLC-MS methods for multiplexed targeted and global metabolic profiling of the urine specimens from the INTERMAP study. The test set consisted of 132 randomly selected samples which included 22 pairs of blinded replicated and different types of quality control samples. Selected metabolites were quantified using the stable isotope labelled internal standards (IS). Both methods were validated according to the FDA guidelines. The quantification results, sensitivity and dynamic ranges were assessed and compared between two methods. The classification ability was MALDI-TOF/MS. Multivariate analysis of the mass spectra of urinary extracts revealed a 2331 Da peptide as a C-terminal PSA fragment. Their quantitative analyses using MALDI-TOF/MS revealed that the peptide may be a new pathognomonic biomarker candidate that can differentiate PCa patients from non-cancer subjects. Those results indicate that the peptide may become a new pathognomonic biomarker for the PCa diagnosis.

CESI-MS as a Tool for Glycosylation Analysis of PSA and Improved Ionization Efficiency with Acetonitrile-enriched Nebulizer Gas

Guinevere S. M. Kammeijer
Leiden University Medical Center

Long Abstract | Bio | Financial Disclosure

A powerful analytical platform for the analysis of biomolecules is capillary electrophoresis – electrospray ionization – mass spectrometry (CESI-MS). Implementation of an acetonitrile-enriched nebulizer gas on the CESI-MS system yielded a more robust platform as well as a gain in sensitivity compared to the conventional platform. The gain in sensitivity could aid in the analysis of samples which are only available in minute amounts. The conventional CESI-TOF/MS revealed region specific accumulation of differently truncated amyloid peptides in various regions of the brain. Moreover, different protein species were selectively regulated in plaque proximity. In conclusion, MS imaging is a promising approach to probe plaque chemistry in Alzheimer’s disease.

Diagnostic and Prognostic Biomarker Discovery of Soft Tissue Sarcomas by Mass Spectrometry Imaging

Sha Lou
Leiden University Medical Center

Long Abstract | Bio

Ability of Matrix-assisted laser desorption/ionization Mass Spectrometry Imaging to distinguish between the most encountered but clinically challenging high grade Soft Tissue Sarcomas (four subtypes) were investigated (leading to diagnostic biomarkers discovery) and if there are individual proteins (signatures) that are statistically associated with patient survival and development of metastases were also investigated (thus would be prognostic biomarkers). Twenty protein peaks were found as diagnostic biomarkers. Fourteen testing, and addition of cortisol to the method. Importantly, we will cover unexpected workflow challenges and continual improvements and discoveries we have made while the assay has been in clinical production.

Serum Aldosterone - An LC Method Development Case Study for a Difficult Analyte (Part 2)

Grace van der Gugten
Providence Health

For the most part, LC-MS/MS assay development and validation is, and should be, a within-laboratory project. However, the new user can find assay development a daunting task. We will describe the LC method development for one of our more challenging to measure endogenous steroids: serum/plasma aldosterone. We will discuss selection of mobile phases, column selection, gradient program
Waters Xevo TQ-S mass spectrometer. Commercially quality control (QC) materials from Chromsystems were used for validation. The method showed good precision, specificity, sensitivity and linearity, and will be useful for clinical research of neurodegenerative disease.

MS method was used for the analysis of the glycoprotein prostate specific antigen (PSA). We were able to identify 50 different N-glycans on a single N-glycosylation site (N69). The used method shows great potential for studying PSA in prostate cancer research to identify disease related alterations of glycosylation in an early stage and therefore could be a promising tool for diagnostic and prognostic evaluation.

Examined on the basis of the multivariate analysis of the global profiles.

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Vitamin D function in the body is partly regulated by catabolism of 1,25-(OH)2D and 25-OH-D by CYP24A1. We have developed a sensitive assay using ACQUITY/TQ-S instruments to quantitate metabolites formed by CYP24A1 including 24,25-(OH)2D3, in addition to 25-OH-D. The talk will focus on the application of our development, interference testing, and addition of cortisol to the method. Importantly, we will cover unexpected workflow challenges and continual improvements and discoveries we have made while the assay has been in clinical production.

**LUNCH**

@ Exhibit Hall / 1st Floor

Lunch to be provided in the Exhibit Hall. • Get ready to join a Corporate Workshop.

**POSTERS**

@ Exhibit Hall / 1st Floor

All Posters to be attended from 1:30 - 2:30 PM.

**CORPORATE WORKSHOPS (2:30 - 3:30 PM)**

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**UPLC-MS/MS-Based Studies of Vitamin D Metabolism: Lessons Learned from CYP24A1 Knockout Mice and Men**

Martin Kaufmann, Queen's University, Kingston Canada

Pre-Register

Vitamin D function in the body is partly regulated by catabolism of 1,25-(OH)2D and 25-OH-D by CYP24A1. We have developed a sensitive assay using ACQUITY/TQ-S instruments to quantitate metabolites formed by CYP24A1 including 24,25-(OH)2D3, in addition to 25-OH-D. The talk will focus on the application of our development, interference testing, and addition of cortisol to the method. Importantly, we will cover unexpected workflow challenges and continual improvements and discoveries we have made while the assay has been in clinical production.

**Mass Spectrometry Applications for Clinical Research**

Dr Robert Graham and Dr Michael Wright

Pre-Register

In this workshop we bring together scientists, clinicians and biochemists that hold an interest in the use of Mass Spectrometry in the areas of Clinical Research as we discuss what can achieved with today’s technology and what we can expect in the future. We have two speakers delivering this workshop. Dr Robert Graham is Senior Lecturer in Clinical Proteomics at the University of Manchester, UK. Dr Graham will discuss protein peaks were found as prognostic biomarkers. Based on comparisons with databases, Acyl-CoA-binding protein, Macrophage migration inhibitory factor, Thioredoxin and Galectin-1 were tentatively assigned among diagnostic biomarkers; Thymosin beta-10, Proteasome activator complex subunit 1, two modified Histone H4 were tentatively assigned among prognostic biomarkers.

**Workshops on Navigating Sample Prep Techniques & Leveraging the Power of Microsampling**

1. Navigating Sample Preparation Techniques in the Clinical LCMS Laboratory

Sean Orlowicz Manager-PhenoLogix

Have you ever asked yourself, "Which Sample Prep Technique is right for this analysis?" If so, you are not alone. In this talk we will investigate, through case studies, some differences between common sample preparation techniques.

2. Leverage the Power of Microsampling to Benefit

**Workshops on Method Automation**

1. Automation and Validation of a SPE Method for the Analysis of 23 Opioids, Cocaine, and Metabolites in Urine with UHPLC-MS/MS

Maria del Mar Ramirez Fernandez, National Institute of Criminology and Criminalistics, Belgium

2. Automated LC-MS/MS methods for Clinical Diagnostics - Realized for Therapeutic Drug Monitoring and Vitamins

Dr. Silvia Bächer, R&D, RECIPE Chemicals + Instruments GmbH

3. Automated SPE Method Development using
The use of advanced accurate mass MS technologies in ovarian cancer biomarker research. We also have Dr Michael Wright, from the Prince of Wales Hospital, Sydney, Australia. Dr Wright is Senior Leader of clinical Chemistry and Endocrinology. In the workshop, he will discuss novel and advanced MS technologies specifically with respect to their use in reducing background and matrix effects in sample analysis.

**Both Your Patient and Your Laboratory**

*James Rudge Ph.D.* - Senior Business Development Manager – Europe

Hospital, clinical, and wellness/biomarker screening labs are using Mitra Microsampling to provide a better, more convenient experience to their patients, while at the same time reducing costs and streamlining workflows. In this workshop, we will discuss the details of an at-home sampling workflow, from collection through analysis, including the optimization and automation of extractions for clinical samples.

**Strata™ – X 96-Well SPE Method Development Plates in Conjunction with a Tecan Freedom EVO® Liquid Handling Platform**

*Sean Orlowicz, Manager-Phenomenex*

Customer experience and commercial insights will be presented for applying automated MS sample preparation in areas of clinical and forensic sample testing, such as therapeutic drug monitoring, DOA, and Vitamin testing. We have pulled together speakers that will present most relevant automated methods and provide guidance on successfully implementing lab established and kit based methodologies.
concentrations in certain patient groups e.g. females with breast cancer. Mass spectrometry is an attractive alternative due to its better specificity and performance at the low concentrations. We have investigated different mechanisms for improving the sensitivity of our current oestradiol assay. Further investigation into the interference of breast cancer medications has shown that one in particular, fulvestrant causes direct interference in two immunoenzymatic assays. The other medications (anastrozole, exemestane and tamoxifen) do not appear to directly interfere. Here we screened mouse serum for metabolic alterations following an acute exposure to gamma radiation using a multi-platform, mass-spectrometry-based strategy. A global, molecular profiling revealed that mouse serum undergoes a series of significant molecular alterations following radiation exposure. We identified and quantified bioactive metabolites belonging to key biochemical pathways and eicosanoids, which could be utilized as an indicator of radiation exposure and as novel target for therapeutic intervention. Monitoring such a molecular response to radiation exposure might have implications not only for radiation pathology but also for countermeasures and personalized medicine.

Targeting Resistance to Proteasome Inhibitor Therapy: A Metabolomics Approach Celia Berkers Utrecht University Long Abstract | Bio Proteasome inhibition has emerged as an important strategy for the treatment of cancer. However, treatment with proteasome inhibitors is often hampered by the occurrence of both primary and acquired resistance. We embarked on unravelling the metabolic mode of resistance to the using species-unique peptide sequences for Apo A-I, Apo A-II, Apo A-IV, Apo B48, Apo B100, Apo C-I, Apo E and Apo J in 3 µl human or murine plasma. In human plasma Apo A-I and Apo A-II showed the highest concentrations. The simultaneous analysis of apoproteins in only 3 µl murine and human plasma allows us a comprehensive characterization of apolipoprotein levels using normo- and hyperlipidemic patients and different mouse strains under different nutritional conditions.

Top-down Mass Spectrometry Methods for Hemoglobin Disorders Diagnosis Didia Coelho Graça University of Geneva Long Abstract | Bio Low and high-resolution top-down mass spectrometry (MS) methods were developed for hemoglobin disorders characterization. An automated workflow using an ion-trap with ETD capabilities allowed to identify the most clinically significant hemoglobin variants and to quantify hemoglobin chains.

Identification and Characterisation of Oxygenated Porphobilinogen Derivatives and their Amino Acid/peptide Conjugates Using Liquid Chromatography-accurate Mass Christopher Benton Agilent Technologies Long Abstract | Bio Financial Disclosure Studying the modification of porphobilinogen is important when trying to understand the pathogenesis of the peripheral neuropathy, chronic renal failure and hepatocellular carcinoma observed in the AHP. Using LCMS analyses (quantitative and qualitative). Examples showing the versatility and the performances of HRMS in HR-full scan will be presented: 1) routine quantification of drugs and endogenous metabolites in plasma extracts, 2) Qual/Quan analysis in a study of the fate of tamoxifen drug in humans and 3) targeted and untargeted metabolomics.

A Sample Preparation Method Development Case Study - Trials and Tribulations with Serum Testosterone (Part 1) Grace van der Gugten Providence Health Use of liquid chromatography-mass spectrometry for analysis of small molecules in clinical laboratories has increased in the past few years. An important component of developing a mass spectrometry method is the sample preparation technique employed in order to sufficiently clean up the sample without develop. Serum phospholipids are present at mg/mL concentrations and contain a charged phosphate group and non-polar fatty acids. This amphipathic structure complicates removal of phospholipids during extraction. Insufficient removal of phospholipids may cause substantial LC-MSMS ion suppression and compromised method robustness -- shortened column lifetimes, shifting retention times, high baselines, and decreased MSMS sensitivity. We will review commonly used LC-MSMS extraction protocols for the ability to concentrate non-ionizable analytes while optimally removing serum phospholipids.
Diagnostic estradiol service is a significant challenge facing many laboratories. In this study, we look at a number of sample extraction options, chromatographic techniques and multistage fragmentation (MRM3) using quadrupole linear ion trap instruments to create robust LC-MS methods that meet the requirements of low level measurement. In this presentation, we propose three different methods to meet the needs of our diverse patient population.

We developed and validated an LC-MS/MS assay for plasma free metanephrines, including 3-MT, and reviewed the analytical and clinical utility of reporting 3-MT over a 1 year period. Performance of the assay in an proteasome inhibitor bortezomib. To this end, we profiled bortezomib-sensitive and -resistant cell lines, combining steady-state metabolomics screens with metabolic flux studies using stable isotope labelling approaches. Our studies revealed that the metabolic profiles of bortezomib-sensitive and resistant cells differed significantly. In particular, resistant cells were more dependent on the uptake of specific nutrients from their environment.

Together, our data indicate a potential role for nutrient starvation in the treatment of bortezomib-resistant tumours.

Analytical performances achieved with this method were compared to gold standard assays used in clinical labs. A high-resolution method was also developed for hemoglobin variants identification. Selected diagnostic product ions were used for fast and reliable data interpretation by non-expert users. MS brings more precise information at the protein level than protein analysis methods currently used for hemoglobin disorders diagnosis.

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external quality assurance scheme was excellent. Clinically, 3-MT was found to be a valuable addition to the profile, providing a useful tumour marker for long term monitoring in one patient. Cabergoline therapy was found to decrease plasma 3-MT, whereas levodopa raised it.

(GNG) on a whole organism scale in diabetes patients, we developed a simple mathematical ODE based dynamic model that considers the main fluxes of (13C labeled) glucose into and out of the blood. In combination with the time-resolved enrichment patterns (Mass Isotopomer Distributions / MIDS) and absolute concentrations of the target metabolites obtained from DBS sampling and GC/MS measurement, we could determine quantitative and robust values for GP and GNG for each studied subject.

Sialylated glycoconjugates by metastable decay and variations in ionization. Here, we present approaches for the linkage-specific sialic acid derivatization of both released glycans and glycopeptides followed by MALDI-TOF-MS analysis. The methods are fast and have an excellent intra- and inter-day repeatability. We envision the use of these methods for the monitoring of protein glycosylation, both in the analysis of biopharmaceuticals and for the detection of glycemic disease biomarkers.

CLOSING RECEPTION

@ Registration Foyer & Front Patio

Enjoy some last bits of time mingling with colleagues. Located in Registration Foyer and Front Patio, weather permitting. Appetizers and drinks to be provided.

Sponsored by:

Thermo Scientific

FRIDAY CLOSED