Short Abstract Listing

Plenary Speaker

O-001

Metabolomics in Drug Development - Pharmacometabolomics

Frank Gonzalez, National Cancer Institute

O-002

Environmental Metabolomics: Past, Present and Future

Mark Viant, University of Birmingham

The field of environmental metabolomics began more than a decade ago with pioneering investigations of the biochemistry of terrestrial and aquatic invertebrates. Since then the field has blossomed into an active research community working across a wide range of applications. This talk will highlight the major challenges that have been addressed successfully in environmental metabolomics, as well as the lessons learned, and discuss some of the current and unsolved issues that lie ahead.

O-003

Metabolomics as a Tool for Plant Breeding

Alisdair Fernie, Max-Planck-Institute of Molecular Plant Physiology

Metabolomics approaches have been documented to have great value in both phenotyping and diagnostic analyses in plants and other species. These tools have recently been turned to evaluation of the natural variance apparent in metabolite composition in both model and crop plants. Here, I will describe exciting progress made in the identification of the genetic determinants of plant chemical composition, focussing on the application of metabolomics strategies and their integration with other high-throughput technologies.

O-004

How to Cheat with Chemometrics

Rasmus Bro, University of Copenhagen

There is no substitute for professionalism! This is a reasonable saying and in a cross-disciplinary field such as metabolomics it is unfortunately often evident that this is still a saying worth reiterating. Cross-disciplinary investigations are complex because competences are needed across a broad range of fields. This often leads to a situation where some are forced to take responsibility of scientific fields they do not fully master. This can have gross impact on results produced and in this talk some of these typical problems are mentioned with a focus on the data analysis part.

Short Abstract Listing

Medicinal Metabolomics

Session Chairs: Rima Kaddurah-Daouk, Don Robertson

O-005

Global Metabolite Profiling Reveals Thymineless Death as an Unexpected Mechanism of Cytotoxicity by the Colon Cancer Chemopreventive Agent Difluoromethylornithine

Steven Gross, Weill Cornell Medical College

Difluoromethylornithine (DFMO) is a chemopreventive drug with efficacy against colon cancer. Although the chemopreventive efficacy of DFMO is considered to arise from ornitine decarboxylase inhibition and consequent depletion of polyamines, how this triggers cytotoxicity is unknown. Using untargeted metabolite profiling, we reveal the broad metabolic consequences of polyamine depletion on cancer cell metabolism, including thymidine-depletion due to metabolic linkage of pathways using S-adenosylmethionine and folate cofactor. Unexpectedly, functional studies demonstrate that thymidine-depletion underlies DFMO cytotoxicity.

O-006

Metabolomics: new opportunities for personalized medicine & pharma

Thomas Hankemeier, Leiden University/NMC

Metabolomics is expected to play an important role in predicting the outcome of pharmacological interventions and to optimize and design multi-dimensional pharmacological interventions. In this presentation examples will be given how to obtain new insights in the working of cardiovascular drugs using a translational approach and how to identify new targets for cardiovascular health and disease using clinical studies.

O-007

A high-resolution lipid profiling study of Lipodystrophy: a systems medicine approach to understanding the mechanistic causes of Insulin Resistance.

Michael Eiden, Medical Research Council - Human Nutrition Research

Lipodystrophy is a comparably rare and unique form of the metabolic syndrome, characterised by general or partial absence of subcutaneous adipose tissue. These patients provide a unique opportunity to evaluate the metabolic consequences of adipose tissue dysfunction, dyslipidaemia and ectopic fat deposition. Here we have compared patients from two severe insulin resistance groups (lipodystrophy and insulin receptoropathy) with healthy, non-diabetic controls using a mass spectrometry based lipidomics approach.

O-008

Understanding and Targeting Metabolism for Drug Discovery in Multifactorial Diseases

Marta Cascante, University of Barcelona

The metabolic flux profile offers a unique opportunity to look at the relationship genotype-phenotype and their interaction with the environment. ISODYN is a computational tool that allows quantifying metabolic flux distributions in living cells offering a flux map that constitutes a distinctive metabolic fingerprint. Here we use ISODYN to understand metabolic adaptations accompanying pathological alterations associated with multifactorial diseases like cancer, diabetes and obesity opening new ways for the development of novel multi-hit therapies.

Short Abstract Listing

Environment & Ecology

Session Chairs: Dan Bearden, Karen Machin

O-009

The importance of genotype in environmental monitoring by metabolomics: applications with the soil super-sentinel organism Lumbricus rubellus

Jake Bundy, Imperial College London

We present results of our ongoing research using metabolomics to monitor the effects of soil pollution in natural field populations of the earthworm species Lumbricus rubellus. When working with natural populations, both site heterogeneity and genetic differences between individuals become of critical importance. The latter is exemplified by the fact that L. rubellus is apparently two or more cryptic species in the UK, with robust metabolic differences between them.

O-010

Metabolomics for Biomonitoring in Waterways Exposed to Wastewater Treatment Plant Effluents

David Skelton, United States Environmental Protection Agency

Metabolomics is now well established for studying contaminant-induced alterations to normal biological function. These alterations have typically been observed in laboratory-controlled studies, but the use of these techniques for biomonitoring in the natural environment has rarely been demonstrated. We have recently conducted biomonitoring studies in waterways near wastewater treatment plants, using caged fathead minnows to demonstrate the utility of metabolomic techniques for characterizing exposures of fish to chemical contaminants.

O-011

Metabolomics reveals key metabolites that convert drosophilid larvae to a freeze tolerant organism

Petr Simek, Biology Centre, Czech Academy of Sciences

The MS-base analysis of the insect larvae metabolome revealed key metabolites involved in the induction of freeze tolerance. Feeding of larvae with labeled metabolites enabled to study their metabolism exposed to cold stress conditions and led to the discovery of a simple strategy which makes an intolerant insect organism freeze tolerant.

O-012

The Investigation into Cheetah (Acinonyx Jubatus) Mortalities at a Captive Breeding Facility In South Africa: Preliminary Findings using a Metabolomic Approach

Adrian Tordiffe, National Zoological Gardens of South Africa

Increased mortalities and clinical illness in adult cheetahs (Acinonyx jubatus) at a captive breeding facility in South Africa were investigated. Serum and urine samples from both healthy and clinically ill cheetahs were collected and analysed for various metabolites using GC-MS and Tandem MS. The preliminary results indicate abnormalities in several metabolites related to the urea cycle in the diseased cheetahs and suggest possible mechanisms for the high incidence of renal disease in this species.

Short Abstract Listing

Human Disease and Health Biomarkers I - Metabolomics in Women's and Children's Health

Session Chairs: Rick Beger, Rick Dunn

O-013

Metabolomics in infant nutrition: metabolic implications of different feeding practices.

Aifric O'Sullivan, UC Davis

The health benefits of breast-feeding have been recognized for some time; however, the underlying mechanisms are still poorly understood. 1H NMR spectroscopy revealed substantial metabolic similarities between rhesus and human infants. In addition, metabolomic profiling of biofluids identified important metabolic consequences of different feeding practices. This study highlights the value of metabolomics in infant nutrition and developmental research.

O-014

An Integrated Study of Biofluids: Metabolic Profiling for Prenatal Health Monitoring

Ana Maria Gil, Department of Chemistry, University of Aveiro

NMR metabonomics of maternal urine and plasma was used to characterise the metabolic trajectory throughout healthy pregnancies; inter-biofluid correlation studies enabled a fuller dynamic metabolic picture to be obtained, with basis on specific urinary and plasma metabolites. Furthermore, an overview of 2nd trimester biofluid composition – amniotic fluid, urine and plasma- is given in relation to several prenatal disorders (preterm, gestational diabetes, premature membrane rupture, malformations, chromosomal disorders) and possible biomarkers and respective validation are discussed.

O-015

Profiling Precursor-Product Ratio In Newborn Screening Of Congenital Adrenal Hyperplasia

Paul Lee, LA Biomedical Reseach Insitute, Harbor-UCLA Medical Center

Newborn screening for inborn errors of metabolism is a powerful application of metabolomics. However, the concentrations of targeted metabolites can be highly variable due to physiological or nutritional influences leading to a large number of false positives results. Profiling precursor to product ratio is a direct interrogation of the functional integrity of the metabolic pathway. The profiling of adrenal steroid ratios is an example of the application of profiling precursor to product ratio in metabolomics.

O-016

Progression to celiac disease is associated with systemic lowering of serum molecular lipids

Marko Sysi-Aho, VTT Technical Research Centre of Finland

We analyzed 161 lipid profiles from 536 samples using semi-quantitative UPLC-QTOFMS platform. The samples were collected prospectively from 15 children ultimately developing biopsy-proven CD during the follow-up (age range 4-121 months, on average 13 samples per child) and from 25 controls matched to the cases by HLA-genotype, gender, birthdate, birth place and sample date. Our results show that there is a strong systemic lowering of lipid levels in patients later developing CD as compared to the healthy controls.

Short Abstract Listing

Plant I - Developments in Plant Metabolomics

Session Chairs: Robert Hall, Lloyd Sumner

O-017

In Vivo Flux Probing of Interactions between Leaf Development and Environmental Stresses

Alexander Erban, Max Planck Institute of Molecular Plant Physiology

The main challenge for plant flux measurements is the in-vivo integration of label, other than CO2, into plants under natural conditions. Aiming to combine the high-throughput of metabolite GC-MS profiling and the systemic information achieved by in-vivo methods, we developed a single-leaf feeding method where labelled precursors are loaded into the plant using a reverse petiole approach. The assay is suitable for plants grown on soil in a phytotron, greenhouse or even in the field.

O-018

Plant metabolomics – PARAFAC2 resolution of bioactive triterpenoid saponins in LC-MS profiles from Barbarea vulgaris and implications for plant-insect interactions

Bekzod Khakimov, Quality and Technology, Department of Food Science, Faculty of Science, University of Copenhage

Multi-way decomposition method PARAFAC2 applied on complex LC-MS data obtained from Barbarea vulgaris plant extracts. PARAFAC2 models developed for the selected regions of the chromatogram enabled resolution and precise quantification of several elusive (e.g. overlapped, elution time shifted and low S/N ratio) peaks. The score values obtained from PARAFAC2 models correspond to relative amounts of the resolved peaks and enabled a good separation between resistant and susceptible plants against the insect herbivore, Phyllotreta nemorum.

O-019

Developing qualitative LC-MS methods for characterizing plant metabolites in NIST Standard Reference Materials (SRMs)

Mark Lowenthal, National Institute of Standards and Technology

Standard Reference Materials (SRM) offer the scientific community a stable source of biomaterial boasting broad application possibilities. Traditionally, SRMs provide quantitative information for only a few targeted analytes. Current efforts attempt to broaden the scope of how and what information is offered to the SRM community by providing qualitative information about biomaterials, such as chromatographic profiles and untargeted metabolite identifications. Here, metabolite profiling is applied to characterizing a suite of Vaccinium berry dietary supplement SRMs.

O-020

Enhancing glycolysis in rice plants under deep water conditions

Miyako Kusano, RIKEN, PSC

Internodes of deep-water rice elongate rapidly in response to partial submergence. The internode elongation of near isogenic line-12 (NIL-12) in a Taichung 65 (T65) background showed 40% internode elongation when compared to that of the deep-water cultivar C9285 by deep-water treatment. To understand relationships between response of internode elongation and metabolomic changes of NIL-12 and C9285, we conducted metabolite and plant hormone profiling analysis of NIL-12, C9285 and the non-deep-water cultivar T65.

Short Abstract Listing

Systems Biology & Pathways

Session Chairs: Alistair Fernie, Villas-Bôas, Silas

O-021

Generating and Curating High-Quality Metabolic Models using Chemical Structure

John May, EMBL-EBI

Creating a high-quality genome-scale metabolite reconstruction requires meticulous manual curation and can take several years to finish. Consequently, many automated pipelines and curation tools have emerged to assist in the process. Despite the tools available, there remains a disconnect, with extensive curation still required on automatically produced 'draft-reconstructions'. We have developed a flexible desktop application (Metingear) that allows development of new and existing models utilising the chemical structure of metabolites.

O-022

Generalized and exact 13C metabolic flux ratio analysis for complex systems

Manuel Hörl, Institute of Molecular Systems Biology, ETH Zurich

We present a novel 13C MFA approach that relies on the acquisition of dense and time-resolved 13C data in the proximity of metabolic nodes, local ODE modeling and parameter estimation by iterative fitting. Based on the outcomes of a study with Bacillus subtilis, we show that this strategy allows estimating relative pathway fluxes on ultra-short time scale considering only local subunits of the cell-wide metabolic network and is suited for complex media and eukaryotic cells.

O-023

Mining the unknown: A systems approach to metabolite identification combining genetic and metabolic information

Jan Krumsiek, Helmholtz Zentrum München

Recent genome-wide association studies (GWAS) with metabolomics data linked genetic variation in the human genome to differences in individual metabolite levels. However, a considerable amount of the molecules currently quantified by modern metabolomics techniques are chemically unidentified. The identification of these “unknown metabolites” is still a demanding and intricate task. We present an approach which integrates GWAS and Gaussian graphical modeling to derive testable hypothesis for the unknown metabolites' identities.

O-024

Super model of the world – Enterococcus faecalis

Carla Portela, University of Auckland

Enterococcus faecalis is a Gram-positive bacterium from the lactic acid group. This natural inhabitant of the gastrointestinal tract is also an opportunist pathogen responsible for various diseases. Recognizing the medical importance of this bacterium, the first genome-scale metabolic model was reconstructed. To support the in silico reconstruction, high throughput omic techniques provided data to validate, test and sustain the robustness of the possible next super model of the bacteria world.

Short Abstract Listing

Understanding Microbial Metabolism with Metabolomics

Session Chairs: Per Bruheim, Masaru Tomita

O-025

In vitro metabolic pathway reveals the action of enzyme effectors

Natsumi Saito, Institute for Advanced Biosciences, Keio University

We designed a method of in vitro metabolic pathways to reveal the effects of small molecules on metabolic enzymes, such as allosteric effectors and metabolic end-products. The method was validated using several amino acid biosynthetic pathways and their feedback control was described. We applied the method to search for effector compounds in the central carbon metabolic pathway and defined the interaction between the pentose phosphate pathway and the TCA cycle by isocitrate-mediated NADPH.

O-026

A novel degradation mechanism, not feedback to CarAB or PyrBI, maintains pyrimidine end-product levels in Escherichia coli

Marshall Louis Reaves, Princeton University

The pyrimidine pathway feedback has long been assumed to enable pyrimidine end product homeostasis. To test this directly, we mutated the genomic copies of CarAB and PyrBI to render them feedback resistant. Using LC-MS, we observed that UTP and CTP levels remained within 20% of wild-type values; however, the feedback resistant strain displayed a profound accumulation of uracil. Thus, we have uncovered a novel homeostatic regulatory mechanism involving disposing of excess pyrimidines.

O-027

Metabolome analysis of Enterococcus faecalis during oxidative stress reveals the role of menaquinone biosynthesis in the oxidative stress management of this bacterium

Silas Villas-Boas, The University of Auckland

The increasing prevalence of multi-antibiotic resistant E.faecalis in hospital acquired infections has prompted reevaluations on the bactericidal actions of conventional antibiotics. Studies have shown that major classes of antibiotics share a common pathway to achieve bacterial cell death by ultimately inflicting oxidative damage to cellular components. Our metabolomics work has provided evidences that menaquinone biosynthesis plays an important role in protecting E.faecalis against oxidative stress.

O-028

Rapid detection and quantification of food spoilage

Roy Goodacre, University of Manchester

Microbiological safety plays a very significant part in the quality control of food products worldwide, and the detection and quantification of bacteria from these foodstuffs is very important for consumer safety. This presentation will report our recent developments in metabolomics, proteomics and spectroscopy for the detection and quantification of bacterial spoilage in food.

Short Abstract Listing

New Technology & Measurements I - Applications

Session Chairs: Dan Bearden, Quincy Teng

O-029

Integration of carbon, nitrogen, and oxygen metabolism in Escherichia coli

Daniel Amador-Noguez, Princeton University

A key challenge for living systems is balancing utilization of different elemental nutrients, such as carbon, nitrogen, and oxygen. We use metabolomics to obtain quantitative understanding of how these systems coordinate with each other in E. coli with a focus on fast-acting regulatory mechanisms. To this end we are: (i) quantifying metabolic responses to nutrient perturbations, (ii) building differential equation models encompassing multiple nutrient systems, and (iii) inferring regulatory principles by combining metabolomics and modeling.

O-030

Direct Analysis in Real Time (DART) for Fast Untargeted Metabolomic Profiling of Human Serum.

Facundo Fernandez, Georgia Institute of Technology

As serum metabolomics is increasingly being used in large scale studies to understand diseases there is a growing need for less time-consuming analytical approaches that are less prone to long term instrument drift. In this work, we demonstrate advances in a new approach for metabolome analysis involving Direct Analysis in Real Time (DART), a plasma-based chemical ionization technique that makes use of reactions with helium metastable atoms to ionize metabolites in a non-contact fashion.

O-031

New Experimental Approaches in Metabolomics with the Nematode C. elegans

Arthur Edison, University of Florida

We are developing new metabolomic protocols using C. elegans in which worms are grown to a defined developmental stage and incubated in water or a defined buffer with defined perturbations. Worms can be isotopically labeled, enabling editing using mass spectrometry or NMR spectroscopy. We will present two novel methods for the metabolomic analysis of worms: MALDI mass spectrometric imaging (MSI) to define the small molecule surface of individual worms and Isotopic Ratio Outlier Analysis (IROA).

O-032

The Application of Hyphenated Thermal Desorption Electrospray Ionisation-Ion Mobility-Mass Spectrometry to the Targeted Analysis of Volatile Biomarkers from Human Skin and Breath

Helen Martin, Loughborough University

A novel approach for targeted screening of volatile organic compounds from human skin and breath has been developed to facilitate higher throughput analysis for metabolomic studies using thermal desorption electrospray ionisation-ion mobility-mass spectrometry. Breath metabolites, with limits of detection under 4µgL-1, have been identified in 10 minutes of analysis. A targeted study of human skin has demonstrated the technique to show qualitative correlation with parallel gas chromatography time-of-flight mass spectrometry analysis.

Short Abstract Listing

Plant II - Plant Physiology and Metabolism

Session Chairs: Ute Roessner, Kazuki Saito

O-033

1H-NMR-MS Metabolomic Analysis of Arabidopsis Uncovers a Novel, Nitrate-Gated, Carbon Flux Safety Valve

Jane L Ward, National Centre for Plant and Microbial Metabolomics

NMR-MS metabolomics analysis of hydroponically grown Arabidopsis has revealed two novel hemiterpenoids that accumulate in leaves in response to root stresses. (Ward et al PNAS, 2011). Under nitrate deficiency or oxidative stress these compounds are formed in coordination with phenylpropanoids in roots. Metabolomics analysis of an array of stress experiments as well as biochemical feeding was used to delineate hemiterpene biosynthetic routes and define a nitrate responsive overflow mechanism for excess photosynthetic carbon.

O-034

Exploiting Chemical Diversity for Triterpene Saponin Gene Discovery in Medicago truncatula

Lloyd W. Sumner, The Samuel Roberts Noble Foundation

Legumes produce an array of natural products that serve critical roles in plant defense, plant-microbe interactions/communication, symbiosis, and human and animal health/nutrition. However, many genes that orchestrate the biosynthesis of natural products still remain unknown. This presentation will describe how metabolomics, correlated gene expression analysis, and genome wide association mapping are being used for the discovery and characterization of triteprene saponin biosynthetic genes in the model legume Medicago truncatula.

O-035

The Role of Hydroxycinnamic Acid Amides for Pathogen Defense of Potato

Melanie Dobritzsch, Leibniz Institute of Plant Biochemistry

In potato, hydroxycinnamic acid amides (HCAAs) are the major secondary metabolites accumulating in response to infection with Phytophthora infestans, the causal agent of late blight disease. To assess the function of HCAAs for pathogen defense in potato, an HCAA transferase gene from Arabidopsis thaliana was expressed in transgenic potato plants. Enhanced HCAA levels were detected in transgenic leaves by metabolite profiling via UHPLC-ESI-QTOF-MS.

O-036

Prediction of freezing tolerance of natural Arabidopsis accessions using metabolomics from field trials and controlled chamber experiments

Ellen Zuther, Max-Planck-Institute of Molecular Plant Physiology

Natural variation in freezing tolerance was phenotyped in 54 Arabidopsis accessions in chamber experiments and 80 accessions investigated in field studies after overwintering. Primary metabolites (GC-MS) were measured and data correlated with freezing tolerance. With PLS regression models metabolites with maximum covariance with freezing tolerance were identified. Good validation of the model was shown with additional accessions under controlled conditions. Such approaches may support marker assisted selection procedures to breed more freezing tolerant crop plants.

Short Abstract Listing

Human Disease and Health Biomarkers II - Understanding Complex Diseases through Metabolomics

Session Chairs: Dan Raftery, Mikhail Bogdanov

O-037

Fumarate hydratase deficient cancer cells exhibit reversed urea cycle activity and excrete the biomarker argininosuccinate

Leon Zheng, Cancer Research UK, Beatson institute.

Loss of function of the tumour suppressor of fumarate hydratase is associated with a highly malignant cancer. The massive accumulation of fumarate has been linked to the tumorigenesis. A metabolomic analyses of urine from Fh1-deficient mice and cell lines is performed. Argininosuccinate is recognized as a significant biomarker. Using stable isotopomer tracing we identified a new biochemical role for the urea cycle enzyme argininosuccinate lyase whereby it operates in reverse direction.

O-038

Targeted Metabolic Profiling of Hepatocellular Carcinoma and Hepatitis C using LC-MS/MS

Hamid Baniasadi, Purdue University

Targeted profiling of serum metabolites was used to differentiate patients with hepatocellular carcinoma and hepatitis C. We analyzed 77 metabolites and identified 16 that were significantly different. A statistical model developed using these 16 metabolites distinguished the two groups with 90% sensitivity and 82% specificity with an ROC curve area of 0.96. These results promise distinguishing between hepatocellular carcinoma and hepatitis C patients and provide insights into the altered metabolic pathways in these two liver diseases.

O-039

Translational Metabolomics and Genomics for Chronic Obstructive Pulmonary Disease (COPD): Discovering a Promising Role for Sphingolipids

Nichole Reisdorph, National Jewish Health

An integrated metabolomics and genomics approach was taken to discover molecular targets of COPD and to determine why only 30% of smokers develop COPD. We identified several novel molecules, including glycoceramides, as emphysema biomarkers in plasma from extensively phenotyped individuals. Parallel genomics revealed that monocytes from smokers with emphysema exhibited marked upregulation of ceramide synthesis enzymes. An animal model demonstrated that ceramides and sphingolipid enzymes are essential components of cigarette smoke-induced lung injury.

O-040

Early detection of Alzheimer's disease in blood and cerebrospinal fluid using metabolomics

Matej Oresic, VTT Technical Research Centre of Finland

Mild cognitive impairment (MCI) is considered as a transition phase between normal aging and Alzheimer’s disease (AD). In a prospective study including healthy controls, MCI and AD patients, we identified a serum biomarker signature comprising three metabolites which was predictive of progression to AD. The major contributor to the predictive model was 2,4-dihydroxybutanoic acid (2,4-DHBA), which was upregulated in AD. We also found that 2,4-DHBA is upregulated in CSF of AD patients, independently of beta-amyloid1-42.

Short Abstract Listing

Plant III - Applied Genetical Metabolomics

Session Chairs: Mike Beale, Robert Hall

O-041

Drought in Wheat: Combining Genetics and Metabolomics to Identify Novel Traits Related to Drought Tolerance

Ute Roessner, The University of Melbourne

In this study we utilize metabolomics to determine drought related metabolite QTL,Äôs in a doubled haploid (DH) population from a cross between drought-intolerant and -tolerant wheat cultivars grown in the field. GC-MS was used to semi-quantify a total of 205 metabolites. Genetic linkage maps and marker scores enabled us to map 217 QTL,Äôs affecting 95 metabolite traits, which we related these to QTLs identified for 29 individual plant growth and yield traits grown under drought.

O-042

Metabolome quantitative trait loci analysis for investigation of genotype–phenotype associations in rice

Kazuki Saito, RIKEN Plant Science Center

A large scale metabolome-quantitative trait loci (mQTL) analysis was conducted to investigate the comprehensive genetic background of metabolic phenotypes in rice grains. The metabolome dataset contains 759 metabolite signals in 85 experimental lines of rice grains Sasanishiki x Habataki back-crossed inbred lines, giving an uneven distribution of 802 mQTLs around the rice genome. Discussion will be given for application of mQTL analysis for rice breeding.

O-043

Identification of metabolites associated with quality traits in barley (Hordeum vulgare) using a non-targeted indiscriminate MS/MS metabolomics approach

Adam Heuberger, Colorado State University

Non-targeted metabolite profiling was performed on barley grain and malt extracts using UPLC-MS to identify metabolites associated with brewing quality traits. Metabolite variation was associated with barley genotype, row-type, growing environment, and genotype-environment interactions. Metabolite-genome interactions were investigated using association mapping with approximately 3,000 SNPs per line. A customized workflow was used to determine metabolite identifications based on indiscriminate MS/MS-level data, and numerous metabolites were identified as candidate markers for malting quality traits.

O-044

Metabolomics-assisted breeding based on metabolite profiling and discovery of key genes of secondary metabolism

Takayuki Tohge, Max-Planck-Institut für Molekulare Pflanzenphysiologie

An LC-MS and GC-MS based global metabolite profiling and microarray analysis were combined to allow comparisons between the relative metabolic levels of leaves, stems, flowers and fruits of S. lycopersicum and seven wild species tomato that can be crossed with it. We will discuss similarities of differences between the levels of variance observed between the different metabolite classes for the purpose of metabolomics-assisted breeding.

Short Abstract Listing

Safety Monitoring and Biomarkers

Session Chairs: Richard Beger, Mike Reily

O-045

Metabolomic Screening for Toxicological and Efficacy Markers in Drug Discovery

Nelly Aranibar, Bristol-Myers Squibb Co.

We report on the development and implementation of a metabolomic screening approach for toxicological and efficacy markers in drug discovery utilizing NMR, LCMS and GCMS analyses. This multimodal approach includes both targeted and non-targeted data profiling, allows confident annotation of over 200 known endogenous metabolites and identifies candidates for follow up with more rigorous quantitative approaches. Identifying drug-related biochemical changes is valuable for assessing unanticipated effects of novel drug candidates or new chemotypes.

O-046

Detection of Idiosyncratic Hepatotoxicity Potential with Metabolite Profiling

Hennicke Kamp, BASF SE

Idiosyncratic drug-induced liver injury (iDILI), where hepatotoxicity occurs in a few individuals treated with a drug that shows no liver injury in routine animal toxicology studies, is a serious concern for both the pharmaceutical industry and regulatory agencies. The question remains whether the potential for iDILI might have been detected in such studies if new measures had been added to the usual complement of clinical and histo-pathology.

O-047

Metabolomics Revealed the Impact of Isonazid on the Endobiotics in Mouse Liver

Feng Li, Kansas University Medical Center

LC-MS based Metabolomic studies suggested that INH has a significant impact on the heme, fatty acyl carnitine, and interaction with fatty acids, which was indentified for the first time. This information may offer a novel avenue in studying the mechanism of INH induced liver injury from an alternate aspect. In addition, this strategy can be applied to the mechanism investigation of the toxicity of other drug.

O-048

Identification of Urinary Biomarkers of Ionizing Radiation Exposure in Non-Human Primates by MS-based Metabolomics

Caroline Johnson, NCI/NIH

Radiation-induced urinary biomarkers were investigated using a non-human primate (NHP) total-body-irradiation model. A time-course of urine samples were collected from NHPs exposed to sham, 1.0, 3.5, 6.5 or 8.5 Gy doses of 60Co-gamma ionizing radiation. They were analyzed by UPLC-ESI-QTOFMS and multivariate data analysis. Thirteen biomarkers were discovered and indicated possible mechanisms for ionizing radiation injury: DNA damage, protection against ROS/cellular injury, protein damage, halting of the beta-oxidation pathway and perturbations to gut microflora.

Short Abstract Listing

Student Session

Session Chairs: Jules Griffin, Jake Bundy

O-049

Metabolite Profiling of Deinococcus radiodurans to Discover the Basis for Radioresistance Conferred by Endogenous Nitric Oxide

Alex Hansler, Weill Cornell Graduate School of Medical Sciences

Deletion of NO synthase (NOS) in the radioresistance eubacteria Deinococcus radiodurans (Drad) diminishes recovery from ionizing radiation. Using metabolomics and other 'omics approaches, we sought to determine the physiological consequences of NOS deletion and determine how endogenous NO confers radioresistance to this bacterium. Our data suggest that NO regulates the membrane/cell wall composition of Drad, in particular affecting the biosynthesis of carotenoid pigments previously hypothesized to mitigate phototoxicity.

O-050

Metabolomics approach for characterizing fatty acid synthesis pathway – a target for brain tumour therapies

Ngoc Ha Dang, University of Calgary

The role of fatty acid synthase (FAS), a key enzyme in fatty acid synthesis, was investigated in glioblastoma multiforme (GBMs) using a metabolomics approach. First, effects of FAS on viability of GBM and metabolic profiles were investigated by targeting cell lines with C75, a slow-binding inhibitor of FAS. Second, FAS was studied as a putative target for glioma invasion due to its observed relationship with the central regulator to the gliomas invasion, neurotrophin receptor p75.

O-051

Chemometric-assisted tool on plant metabolomics: Chemotypes distribution from Solanum species using PARAFAC-HCA method.

Alan Pilon, Institute of Chemistry-UNESP

In plants, the complex nature of the crude extracts (genetic variability, development stages, environment changes) contributes to difficulty on metabolomics studies. In this work we developed a method to determine the metabolic distribution for Solanum genera using structural features of molecules available in the literature, based on PARAFAC-HCA. This tool was helpful to metabolomics by assisting chemotype composition of an unknown organism, based on micromolecular comparison with another related species.

O-052

Fast and sensitive metabolic profiling of very polar metabolites using HILIC chromatography and capillary-flow UPLC-MS

David Jonathan Fischer, Functional Genomics Center Zurich

Using capillary flow and ultrahigh performance LCMS, we developed a fast and sensitive quantification method for very polar metabolites in a non-targeted approach (fullscan accurate mass spectrometry).

O-053

Metabolomic profile of colorectal cancer patients shows reproducibility in pre-operative and intra-operative conditions

Farshad Farshidfar, University of Calgary, Faculty of Medicine

Colorectal cancer patients should be diagnosed early to benefit from the treatment options, and serum metabolomic profile may detect early disease. General anesthesia may change this profile. It was interesting for us to see how metabolomic profile changes after induction of the anesthesia. Forty five samples in 3 groups of pre-operative, intra-operative and matched control were analyzed with GC-MS. Our findings show a very similar metabolomic profile is evident in pre-operative and intra-operative serum profiles.

Short Abstract Listing

Student Session

Session Chairs: Jules Griffin, Jake Bundy

O-054

Maternal urine metabolic profiling: a means to follow the metabolic adaptations throughout pregnancy and predict prenatal disorders

Silvia Oliveira Diaz, Department of Chemistry, University of Aveiro

This work describes an NMR metabonomic study of maternal urine to evaluate the dynamic metabolic adaptations throughout pregnancy. A selection of 21 metabolites was found to describe the time trajectory of healthy pregnancies, setting the basis to detect deviating trajectories in case of prenatal pathologies. A parallel study of 2nd trimester maternal urine unveiled possible urinary markers for fetal malformations and chromosomal disorders and potential predictive markers for gestational diabetes mellitus and preterm delivery.

Short Abstract Listing

Databases & Data Analysis

Session Chairs: Christoph Steinbeck, Eldon Ulrich

O-055

MetaboLights: a Database for Metabolomics Experiments and Derived Information

Kenneth Haug, European Bioinformatics Institute

MetaboLights is a database for metabolomics experiments and the associated metadata. It is the first comprehensive, cross-species, cross-platform/technique database which combines curated reference data of pure metabolites, curated information about their occurrence and concentration in species, organs, tissues and cell types under various conditions with data characterizing the experiment which lead to these findings and allows ready cross-referencing between experiments. Protocols documenting how metabolomics experiments were conducted are also available.

O-056

MzMatch/mzMatch.R: an Open Source Software for the Sequential Processing and Analysis of Mass Spectrometry Data

Andris Jankevics, Groningen Bioinformatics Centre, University of Groningen

Liquid Chromatography Mass Spectrometry (LC-MS) is a powerful and widely applied method for the study of biological systems, biomarker discovery and pharmacological studies. Here we present our customizable pipeline for mass spectra calibration, processing, filtering, annotation, statistical analysis and visualization. We illustrate the application of the mzMatch pipeline in a variety of large metabolomics studies, ranging from work on bacterial cell extracts to human biofluids and cancer cells.

O-057

Metabolomics Using an Automated Metabolite Identification Pipeline

Julio Peironcely, TNO Research Group Quality & Safety

In order to assist metabolite identification, we have developed computational tools to process and compare multi-stage mass spectrometry (MS) data, to elucidate the chemical structure of metabolites, and to filter unrealistic structures. These tools have been integrated in an pipeline and used to identify metabolites present in human urine. The results of using such a metabolite identification pipeline for urine metabolites will be presented.

O-058

Differential Correlation Networks as Complex Phenotypes in Metabolomics

Timothy Ebbels, Imperial College London

Metabolite correlation networks are often used to interpret metabolomics experiments. But how do these networks change across biological states? We introduce a statistical method for the differential analysis of correlations and illustrate our approach with a large NMR lipoprotein dataset from individuals with and without prediabetes. Using the new method we identified several changes related to diabetic dyslipidemias which were not detected by conventional techniques, thus providing an complementary view of the complex metabolic phenotype.

Short Abstract Listing

Nutritional Metabolomics

Session Chairs: Isabel Bondia-Pons, Vijayalakshmi Varma

O-059

Regulated, Non-Stochastic Modulation of the Fatty Acyl Composition of Rat Liver Mitochondrial Cardolipins in Response to Diet

Bruce Kristal, Brigham and Women's Hospital

Cardiolipins (CL) are a family of phospholipids essential for mitochondrial structure and function. We examined diet-mediated changes in liver mitochondria from male FBNF1 rats fed 24 different low-fat, isocaloric diets. Growth rates and core mitochondrial functions were essentially unaffected, but mass spectrometry-based, mitochondrial lipidomics profiling revealed up-regulation of CLs in rats fed saturated or trans fat-based diets with a high glycemic index. This study reveals unexpected complexity/regulation of the central lipid in mitochondrial metabolism.

O-060

Discovery of Metabolomics Biomarkers of Nuts Consumption to Decipher the Role in the Improvement of the Metabolic Syndrome Status

Cristina Andres-Lacueva, Biomarkers and Nutritional & Food Metabolomics Research Group Department of Nutrition and Food

Using a LC-ESI-qToF/ITD-FTMS approach we explored metabolome modifications in MetS-subjects following 12w nuts consumption. Among potential markers of nuts intake, serotonin, fatty acids and polyphenols metabolites were identified. Insulin resistance, inflammation, adiposity and oxidative stress parameters were measured, relationships between metabolomics biomarkers and MetS status investigated, and responsive and nonresponsive metabotypes explored. Results confirmed how untargeted metabolomics may help accessing unexplored pathways impacted by diet.

O-061

A data driven strategy to discover dietary biomarkers and validate new diet recording tools suitable for epidemiological studies

John Draper, IBERS

Diet has a major effect on health but it has proved difficult to demonstrate causative relationships between consumption of specific foods and a reduction in the risk of major chronic disease. Non-targeted metabolite fingerprinting and machine learning can identify dietary biomarkers in post-prandial urines. We now describe a data-driven procedure to determine which food components are appropriate for biomarker development and demonstrate how to validate new quantitative dietary assessment methods suitable for large-scale population surveys.

O-062

Metabolomics Analysis of Cultured HepG2 Liver Cell Line Reveals Fructose Structure and Hexose Concentration Dependent Changes in Metabolite Profiles

John Meissen, UC Davis

We applied a metabolite profiling approach, including both GC-TOF and HILIC-QTOF MS profiling strategies, to better define the metabolic impact of fructose consumption in human liver tissue. Metabolite extracts from cultured HepG2 cells incubated in media containing fructose were compared with controls incubated in media containing two different concentrations of glucose. Comparison of all 156 annotated metabolites with MetaMapp metabolite networks revealed shifts in metabolite abundance based on both hexose structure and hexose concentration.

Short Abstract Listing

Human Disease and Health Biomarkers III - Pathophysiology and Metabolic Pathways

Session Chairs: Ana Maria Gil, Matej Oresic

O-063

Liver fat changes the metabolic flexibility of the liver in non-alcoholic fatty liver disease

Tuulia Hyotylainen, VTT technical research centre of Finland

A global metabolomics approach was applied for prediction of non-alcoholic fatty liver disease (NAFLD) and liver fat, and for characterization of metabolic fluxes across the splanchnic bed in human fatty liver, followed by transcriptomic study in human liver biopsies. Our results indicate that (1) serum metabolomics can help in determination of liver fat, (2) in diagnosis of NAFLD and (3) several metabolic pathways are associated with NAFLD progression, opening potential novel therapeutic avenues.

O-064

Quantitation of Intracellular Metabolic Fluxes in Cancer Cell Lines

Jing Fan, Princeton University

Oncogenes promote uptake of nutrients including glucose and glutamine to support tumor growth. The effect of specific oncogenes on intracellular metabolic activity, however, remains less well understood. To address this, we developed methods that combine isotope tracers, LC-MS analysis, and redox and cofactor-balance constraints to quantitate intracellular fluxes in a variety of cancer cell lines.

O-065

ATP-related 1H/13C NMR Metabolomic Analysis in a Neonatal Rat Brain Slice Model of Oxygen-Glucose Deprivation Followed by Mild Hypothermia Treatments

Jia Liu, University of California, San Francisco

This study investigated the effects of mild hypothermia on the metabolic pathways and interaction between neurons and glia in superfused neonatal cerebrocortical slices injured by OGD. We analyzed perchloric acid extracts of pre- and post-OGD slices with 21.1 Tesla 1H/13C NMR–based metabolomics. Metabolite data sets can distinguish treatment groups as well as early and late outcomes. Several key metabolites were identified to closely correlate with the changes of ATP.

O-066

NMR Metabonomics of Blood Plasma and Urine: Potential in Lung Cancer Screening and Diagnosis

Iola Duarte, University of Aveiro

Multivariate modeling of NMR data from either blood plasma or urine allowed differentiating between lung cancer and healthy subjects with sensitivity and specificity above 90%. In spite of possible confounding factors (e.g. age, smoking status), a number of metabolites were found to be consistently altered in the biofluids of patients, suggesting a systemic metabolic signature for lung cancer and showing the potential of NMR metabonomics for the minimally invasive detection and monitoring of the disease.

Short Abstract Listing

New Technology & Measurements II - Technology

Session Chairs: Thomas Hankemeier, Du Toit Loots

O-067

High-Resolution Metabolomics to Operationalize the Exposome

Dean Jones, Emory University

Dual chromatography high-resolution mass spectrometry, apLCMS and msAnalyzer are used to routinely measure 44,000 ions in a 20 min analysis of human plasma, including matches (5 ppm) to more than half of KEGG human metabolites and products of the microbiome, drugs and environmental agents. The data suggest that high-resolution metabobolomics with resolution comparable to that for the human genome can quantify life-course environmental exposures from the prenatal period onwards as conceptualized in the exposome.

O-068

Characterization of coularray identified plasma metabolite biomarkers using LC-UV fractionation and MS and NMR-based detection

Susan Bird, Brigham and Women's Hospital

LC separation combined with coulometric-electrode array detection can sensitively and robustly profile and identify electrochemically active biomarkers of interest that differentiate an individual’s nutritional status and reflect disease risk. This method cannot, however, structurally-characterize the metabolites that comprise these profiles. Through offline plasma concentration and fractionation, MS and NMR-based analytical methods are used to characterize these unknown metabolites, providing the unambiguous identifications necessary to move past biomarker discovery and define their biological and clinical importance.

O-069

Push-through Direction Injection NMR Automation

Quincy Teng, US Environmental Protection Agency

We have developed a push-through direct injection (PT DI) NMR method in 96-well plate format to increase the throughput of NMR experiments. This new technique overcomes all known problems with conventional DI NMR methods. The automation of thousands of samples has proven that the new PT DI NMR technique is reliable, efficient, and free of carryover contamination and sample diffusion.

O-070

microRNAs act in parallel to insulin/IGF-1 signalling to control healthspan and ageing in Caenorhabditis elegans

Cecilia Castro, Department of Biochemistry

Acute inactivation of miRNA synthesis specifically in Caenorhabditis elegans adult animals was studied by a comprehensive metabolomics approach. The impact on the organism in terms of metabolism, and on lipids in particular, is profound, revealing that mutant animals have a distinct metabolic profile and showing changes in PUFA, highly unsaturated phosphocholines and free PUFA. This is particularly timely as there is increasing evidence that microRNAs are important regulators in glucose homeostasis in mice.

Short Abstract Listing

Funding Opportunities and International Initiatives

Session Chairs: Young Kim, Christoph Steinbeck

O-071

National Institutes of Health- Common Funds Metabolomics Research Opportunities

Philip Smith, National Institute of Diabetes, Digestive and Kidney Diseases

This presentation will cover the range of resources and infrastructure, being supported by NIH Common Funds program, that include comprehensive cores that provide metabolomics services, data repository coordination, technology development, development of standards, workforce development. In addition, there will be discussion on how these can be resources can be leveraged for advancing international metabolomics research.

O-072

Funding Opportunities at the National Science Foundation

Jane Silverthorne, National Science Foundation

The U.S. National Science Foundation (NSF) supports basic research and education in science and engineering. It is the only federal agency whose mission includes support for all fields of fundamental science and engineering, except for medical sciences. Unlike many other federal agencies, NSF does not hire researchers or operate its own laboratories or facilities. Instead, researchers are supported directly through their own home institutions, which are typically universities and colleges. In this talk, funding opportunities with relevance to basic research in metabolomics as well as national and international collaborations will be presented.

O-073

Bioplatforms Australia – an initiative to translate 'omics technologies to systems biology

Ute Roessner, The University of Melbourne

The National Collaborative Research Infrastructure Initiative established Bioplatforms Australia, a national technology consortium to provide the analytics and informatics delivering "Systems Biology" to research and industry. This investment made over 7 years involves 4 platforms including Genomics Australia, Proteomics Australia, Metabolomics Australia and Bioinformatics. In order to demonstrate the concept, pilot studies have been initiated around national research priorities utilising the integrated capabilities of all BPA platforms to establish a comprehensive systems-based model and information collection.

O-074

Canadian Initiatives and Innovations in Metabolomics

David Wishart, University of Alberta

In this presentation I will describe some of the recent activities being conducted in Canada in metabolomics. In particular, I will provide an update on the Human Metabolome Project and the efforts to systematically characterize and compile data on various human biofluids and the different metabolomes found in humans. I will also describe the newly established Metabolomics Innovation Centre (TMIC) which is serving as Canada's national metabolomics platform.

Short Abstract Listing

Workshop - Software Showcase

Session Chairs: Steffen Neumann, Sandra Castillo

O-075

Generation of numerical data matrices for marker search within large-scale GC-(TOF)-MS profiling experiments using TagFinder

Alexander Erban, Max Planck Institute of Molecular Plant Physiology

Metabolic profiling and fingerprinting studies become larger and more complex since robustness of instrumental data acquisition improved substantially within the last years. Therefore, screenings for metabolic markers which employ large-scale and highly replicated profiling studies are getting more and more frequent. In this study were explore the options and limitations of the assembly of large numerical data matrices from GC-TOF-MS metabolite profiling experiments using the TagFinder software.

O-076

Comparative evaluation of software for analysis of GC-MS metabolomics data

Brian McGarvey, Agriculture and Agri-Food Canada

Data analysis in metabolomics experiments using GC-MS normally includes deconvolution of chromatographic peaks, alignment of chromatographic peaks, peak picking and area integration, statistical analysis, and chemical identification of statistically significant chromatographic peaks. This work reports a comparative evaluation of the performance of nine software packages developed in recent years to automate several or all of these steps using lab-prepared mixtures of chemicals as well as a plant extract spiked with a mixture of alkanes.

O-077

Identification of unknown compounds in GC-MS based Metabolomics: A case study applying GC-APCI-Q-TOF analysis combined with in-silico fragmentation tools

Aiko Barsch, Bruker Daltonik GmbH

The benefits of high resolution MS data in combination with GC separations for structure elucidation will be demonstrated based on plant and bacterial metabolomics example. A GC-APCI interface preserves the pseudomolecular ion information and enables elemental formula generation. Combined with in-silico fragmentation tools to compare accurate mass Q-TOF MS/MS information with possible fragment structures allows to identify ‚Äúknown unknowns‚Äù without the need of reference MS/MS spectra.

O-078

MZmine 2: Open-source framework for processing mass spectrometry based data

Sandra Castillo, VTT

MZmine 2 is a platform-independent software developed using Java technology. MZmine 2 allows processing, visualization and analysis of high-resolution mass spectrometry data. It has been recently integrated with the statistical computing environment R to allow the possibility of using algorithms available in R. A future goal is to add the possibility of importing peak lists not associated with any raw data allowing us to work with data that has been partially processed by other software.

O-079

Mass Spectrometry in KNIME: Custom Nodes for Data Pre-Processing

Stephan Beisken, European Bioinformatics Institute

We have developed a novel, easy-to-use tool for mass spectrometry (MS) metabolomics data pre-processing. The tool is integrated in the publicly available and free of charge workflow environment KNIME. Workflow-driven MS data analysis helps the user to explore the data acquired after every processing step, while still being able to easily go back and forth between the individual steps and adjust the given parameter sets.

Short Abstract Listing

Workshop - Software Showcase

Session Chairs: Steffen Neumann, Sandra Castillo

O-080

MetaboAnalyst 2.0 & ROCCET – web-based tools for comprehensive metabolomics data analysis and biomarker discovery

Jianguo Xia, University of Alberta

We present MetaboAnalyst 2.0 and ROCCET - two freely available and easy-to-use web applications for metabolomics data analysis and biomarker discovery. MetaboAnalyst 2.0 represents a significant improvement over its original version in almost every aspect - data processing, statistical analysis and functional interpretation, along with many new features and enhanced user interface. ROCCET is designed to perform various common tasks for robust biomarker identification and their performance assessment.

Short Abstract Listing

Workshop - Analytical QC Measures for Interlaboratory Comparability

Session Chairs: Dan Bearden, Mark Viant, Laura Schnackenberg

O-081

The role of quality control (QC) samples in untargeted metabolomics: emergence, quality assurance and data pre-processing

Warwick Dunn, University of Manchester

The assessment of data quality in untargeted metabolomic studies is an essential requirement for metabolomics to be widely accepted in the scientific research community. However, the incorporation of QC samples in to metabolomic studies is currently not widespread. This presentation will discuss the emergence of QC samples in these studies, experimental approaches for sample preparation and analysis, quality assurance of data and signal correction applying QC data.

O-082

eMICE 2011 – An Environmental Metabolomics Intercomparison Exercise

Dan Bearden, National Institute of Standards and Technology

A second multi-national exercise was conducted involving 12 participating laboratories resulting in 16 data sets from instruments operating at 4 different magnetic field strengths from 500-800 MHz. This presentation will provide an extensive analysis of the second intercomparison results and we will discuss our experience coordinating two large-scale metabolomics intercomparison exercises.

O-083

Optimized Analytical Quality of Direct-Infusion Mass Spectrometry-Based Metabolomics

Ralf Weber, University of Birmingham

High-resolution direct-infusion mass spectrometry (HR DIMS) is a technique used in metabolomics to simultaneously measure large number of small molecules. It provides high-throughput screening and is therefore increasingly used for sample classification. We will provide both the novice and the experienced MS user with a broad overview of the current bioinformatics approaches and challenges involved in performing HR DIMS-based metabolomics. The bioinformatics workflow presented has been successfully applied in environmental as well as medical-based research.

O-084

NIST Standard Reference Materials (SRMs) as Quality Control for Use in Validating Metabolomic Sample Processing

Tracey Schock, National Institute of Standards and Technology

The metabolomics sample processing step can be influenced by variations in extraction procedure, materials contamination, multiple personnel and the length of time between extractions of sample batches. NIST standard reference materials (SRMs) are ideal quality control materials for sample processing that permits evaluation of extraction technique reproducibility and the results can be compared between projects or laboratories in subsequent research providing long-term comparability and confidence in the data.