18e JOURNÉES SCIENTIFIQUES

Réseau Francophone de Métabolomique et Fluxomique

LILLE, 19 - 22 MAI 2026

RFMF Lille 2026

LILLE GRAND PALAIS
ATELIERS - INSTITUT GERNEZ RIEUX

http://18-js-rfmf-2026.sciencesconf.org

RFMF
Réseau Francophone de Métabolomique et Fluxomique

Egid · PreciDIAB National Center for Precision Diabetic Medicine · Université de Lille · CHU Lille · BioEcoAgro · hellolille · MEL Métropole Européenne de Lille

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Swiss Institute of Bioinformatics

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Université de Lille

MÉTROPOLE EUROPÉENNE DE LILLE

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Partenaires industriels Silver des 18èmes Journées Scientifiques du RFMF

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EGID : U1283 INSERM UMR8199 CNRS, Institut Pasteur de Lille, CHU de Lille, Université de Lille, European Genomic Institute for Diabetes, Université de Lille
RD3-PBM : Unité RD3-Pharmacognosie, Bioanalyse et Médicaments (RD3-PBM) & Plateforme analytique de la Faculté de Pharmacie (APFP), Université libre de Bruxelles (ULB), Bruxelles, Belgique
PRISM : U1192 Protéomique, Réponse Inflammatoire et Spectrométrie de Masse (PRISM), Université de Lille
CIRM : Metabolomics group, Center for Interdisciplinary Research on Medicines (CIRM), University of Liège, Belgium
BioEcoAgro : UMRT INRAE 1158 BioEcoAgro Lille, Université de Picardie Jules Verne, Amiens
GRITA : ULR 7365 GRITA, Université de Lille

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- David Touboul, Laboratoire de Chimie Moléculaire, Ecole Polytechnique, IP Paris, Palaiseau (91), France

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- Jérémy Monteiro, Plateforme de Métabolomique et d'Analyse Chimique - MetaboHub Tours, US 61 INSERM CHRU Université de Tours, Tours (37), France

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Ateliers scientifiques

Découvrir Galaxy W4M

Personne(s) encadrant l'atelier :

- workflow4metabolomics
- Cédric Delporte
- Yann Guitton

Public envisagé et les prérequis :

- Public : Tout public avec ou sans expérience en traitement de données métabolomique
- Prérequis : Avoir envie d'en savoir plus sur Galaxy Workflow4Metabolomics ou avoir des questions à poser aux experts

Objectif de l'atelier :

Cet atelier a pour objectif de faire découvrir les outils de traitement de donnée (MS(/MS) et RMN) et d'analyses statistiques disponibles sur W4M - Galaxy. Les participants repartiront avec une vision d'ensemble des outils et des supports d'auto-formation. Le profil des participants est plutôt «débutant.e.s» dans l'analyse de données sur Galaxy-W4M (aucun prérequis nécessaire). Au programme : Introduction à W4M et de ses outils, suivie d'une session questions/réponses.

Durée de l'atelier : 2h

Date et lieu : Mardi 19 mai de 14h à 16h à l'institut Gernez Rieux (CHU Lille)

Nb de places maximum : 40 personnes

Nettoyage de données GC & LC-MS avec Cinderella

Personne(s) encadrant l'atelier :

- Goddard Mary-Lorène
- Lacrampe Nathalie

Public envisagé et les prérequis :

- Public : Tout public
- Prérequis : Avoir déjà manipulé des données de métabolomique

Objectif de l'atelier :

Cet atelier pratique a pour but d'apprendre à utiliser CINDERELLA, un outil R avec une interface utilisateur conviviale, permettant d'éliminer les artéfacts de manière semi-automatique et supervisée. A partir d'un jeu de données brutes pré-processées issues d'analyses GC ou LC-MS (table d'aires/intensités des features dans les échantillons) et des métadonnées, nous apprendrons à utiliser l'application R Cinderella pour 1/ imputer les valeurs manquantes, 2/ réaliser des normalisations, 3/ corriger les dérives analytiques et 4/ filtrer les artéfacts et les signaux peu pertinents biologiquement dans le but d'obtenir des données de qualité avant de réaliser des analyses statistiques. Cet atelier sera aussi l'occasion d'échanger autour des pratiques et besoins de chacun concernant le nettoyage des jeux de données de métabolomiques par spectrométrie de masse.

Durée de l'atelier : 2h

Date et lieu : Mardi 19 mai de 14h à 16h à l'institut Gernez Rieux (CHU Lille)

Nb de places maximum : 30 personnes

Vibe coding pour la métabolomique

Personne(s) encadrant l'atelier :

- Touboul David
- Wisson Robin
- Amoros Camille
- Butin Noémie

Public envisagé et les prérequis :

- Public : Tout public
- Prérequis : Connaissance en métabolomique, aucun pré-requis en informatique/ programmation

Objectif de l'atelier :

L'objectif de cet atelier est de démocratiser la création d'outils d'analyse en métabolomique via le vibe coding : une approche itérative où l'on formule ses besoins en langage naturel et où des agents IA génèrent, testent et améliorent du code en direct. Nous montrerons comment cette méthode peut réduire de plusieurs ordres de grandeur le temps et l'expertise nécessaires pour prototyper une application d'analyse.

La partie "concepts" couvrira : bonnes pratiques de prompts, structuration d'un mini-projet, tests rapides, traçabilité (git), et surtout garde-fous scientifiques (validation, reproductibilité, limites).

La partie pratique sera un live coding dans VS Code (idéal pour débuter) pour construire pas à pas un mini-outil métabolomique (lecture de données, pré-traitements/QC, normalisation, analyses simples et visualisations).

Durée de l'atelier : 2h

Date et lieu : Mardi 19 mai de 16h à 18h à l'institut Gernez Rieux (CHU Lille)

Nb de places maximum : 30 personnes

Améliorer l'identification des métabolites et leur intégration dans un contexte multiomique : utilisation de la ressource MetaNetX

Personne(s) encadrant l'atelier :

- Mehl Florence
- Pagni Marco

Public envisagé et les prérequis :

- Public : Tout public
- Prérequis : Pas de prérequis particulier

Objectif de l'atelier :

L'atelier a pour ambition de montrer comment utiliser efficacement la plateforme MetaNetX dans une approche centrée sur les métabolites, en particulier pour la conversion, la normalisation et la réconciliation des identifiants issus de différentes bases de données ou de réseaux métaboliques. Les participants découvriront comment exploiter les services de mapping de MetaNetX pour passer aisément d'identifiants d'une ressource (KEGG, ChEBI, BiGG, SEED ou HMDB) à une autre. L'atelier illustrera comment ces mappings peuvent être intégrés dans des pipelines de curation ou utilisés pour améliorer la qualité, la cohérence et la complétude d'une base de données interne, notamment lors de la construction ou de l'annotation d'un modèle métabolique. À travers des exemples pratiques, nous montrerons comment résoudre les ambiguïtés entre synonymes et structurer une base interne autour d'identifiants harmonisés. Enfin, l'atelier visera à discuter des bonnes pratiques et des limites actuelles, tout en recueillant les besoins des utilisateurs pour les futures évolutions de la ressource.

Durée de l'atelier : 2h

Date et lieu : Mardi 19 mai de 16h à 18h à l'institut Gernez Rieux (CHU Lille)

Nb de places maximum : 30 personnes

Atelier Junior

Personne(s) encadrant l'atelier :

- Léo Andruszkow
- Nathalie Lacrampe
- Axelle Bourez

Public envisagé et les prérequis :

- Public : Jeunes scientifiques en métabolomique et fluxomique
- Prérequis : < 33 ans au 01/01/2026

Objectif de l'atelier :

Cet atelier a pour but de créer des liens entre les jeunes scientifiques (étudiants, doctorants, post-doctorants, techniciens, ingénieurs, chercheurs …) du RFMF junior afin de promouvoir et faciliter les échanges inter-laboratoires lors de l'atelier et tout au long des JS.

Ainsi, après une activité brise-glace, plusieurs groupes de 6 personnes, accompagnés par un membre senior du RFMF, seront amenés à imaginer un projet de recherche en combinant les compétences des membres du groupe et devront établir un budget prévisionnel, construire une timeline, proposer une projection de valorisation et réfléchir à l'impact environnemental du projet.

Cet atelier se déroulera au cours de la pause déjeuner, des boissons ainsi qu'un repas (de type pizza) seront proposés. Au cours de l'atelier, un canal Slack sera créé afin de favoriser les échanges conviviaux tout au long des journées scientifiques.

Durée de l'atelier : 2h

Date et lieu : Mardi 19 mai de 12h à 14h à l'institut Gernez Rieux (CHU Lille)

Nb de places maximum : 30 personnes

Atelier mentorat

Personne(s) encadrant l'atelier :

- Corentine Goossens
- Chloé Cloteau
- Nathalie Lacrampe
- Rochelle Kouakou

Public envisagé et les prérequis :

- Public : Tout public
- Prérequis : S'être inscrit.e via le formulaire pour faire partie de la prochaine édition

Objectif de l'atelier :

Clôture de l'édition 2025-2026 et lancement de la prochaine édition 2026-2027 de programme de mentorat.

Après une brève présentation et des retours d'expérience du programme de mentorat, l'atelier sera consacré aux échanges entre les binômes mentor / mentoré(e).

Durée de l'atelier : 1h45

Date et lieu : Jeudi 21 mai de 17h à 18h45 à Lille Grand Palais

Nb de places maximum : 50 personnes

Programme détaillé par journée

MARDI 19 MAI 2026

Ateliers — Institut Gernez Rieux (CHU Lille)

09h00 - 12h00 **CA RFMF**
12h00 - 14h00 Atelier Junior
14h00 - 16h00 Atelier "*Découvrir Galaxy W4M*"
14h00 - 16h00 Atelier "*Nettoyage de données GC & LC-MS avec Cinderella*"
16h00 - 18h00 Atelier "*Vibe coding pour la métabolomique*"
16h00 - 18h00 Atelier "*Améliorer l'identification des métabolites et leur intégration dans un contexte multiomique: utilisation de la resource MetaNetX*"

MERCREDI 20 MAI 2026

Lille Grand Palais

09h00 - 09h20 **Bienvenue**
09h20 - 10h05 **Plénière 1 :** Lynn Vanhaecke
From gastrointestinal metabolomics to pediatric precision medicine through source-based metabotyping

10h05 - 10h25 **Communications orales :**
O1 - Martin Jean-Charles
Xtremomics ou exploration métabolomique de l'adaptation humaine aux environnements extrêmes

10h25 - 11h00 **Pause + Posters**

11h00 - 11h40 **Communications orales**
O2 - Da Silva Célie
Multiblock Chemometric Approaches to Decode Multisource Molecular Signatures of Perceived Stress in Healthcare Students
O3 - Pagni Marco
Integration of Heterogeneous Biochemical Knowledge and Assembly of the Next Reconstruction of Human Metabolism with a Focus on Lipids

11h40 - 12h00 **Flashs session 1**
F01 - Defauwes Inès
Study of the impact of storage conditions on the stability of metabolites in fecal samples for 1H NMR metabolomics analysis
F02 - Boissin Louise
Steroidome quantification by online SPE for LC-HRMS: towards a systematic application in endometriosis research
F03 - Strassel Oriane
Surrogate Internal Calibration Strategies for Extended Absolute Quantification by LC-MS/MS
F04 - Delage Marie
Integration of 1D and fast 2D (UF-COSY, NUS-HSQC, NUS-TOCSY) NMR metabolomic and lipidomic datasets applied to mice liver samples

12h00 - 14h00 **Repas midi + Posters**

14h00 - 14h45 **Plénière 2 :** Cédric Bertrand

Environmental Metabolic Footprinting (EMF) : Une approche métabolomique pour évaluer le devenir et l'impact des mélanges chimiques complexes

14h45 - 15h45 **Communications orales**

O4 - Diémé Binta

Integrating metagenome-scale metabolic modelling and metabolomics to identify metabolic interactions in Microcystis phycospheres

O5 - Pinheiro-Costa-Pimentel Mariana

Predictive metametabolomics unravels environmental drivers of spatial heterogeneity of microbial metabolome assemblage in aquatic peripthyon

O6 - Campas Manon

One-year longitudinal follow-up to assess intra- and inter-individual metabolite variations in healthy volunteers

15h45 - 15h55 SPONSOR - THERMOFISHER

15h55 – 16h25 **Pause + Posters**

16h25 - 17h25 **Communications orales**

O7 - Terra Charles

Comparative Untargeted Metabolomic Profiling Reveals Virus-Specific Metabolic Reprogramming in Human Airway Epithelium Infected with SARS-CoV-2 and Influenza A Virus

O8 - Myridakis Antonis

Simultaneous targeted quantification and untargeted discovery of human serum metabolome: SQUAD Metabolomics

O9 - Grovel Olivier

Eco-inspired multicultures for the discovery of new antiobiotics from marine fungi

17h25 - 17h45 **Flashs session 2**

F05 - Mekbel Katia

Du champ à l'assiette: transfert des effets du génotype et des procédés de transformation du colza sur la santé animale et humaine dans une approche One Health

F06 - Brosse Céline

Uncovering the diversity and ecological roles of glucosinolates in rapeseed seed exudates

F07 - Saccaram Chandrodhay

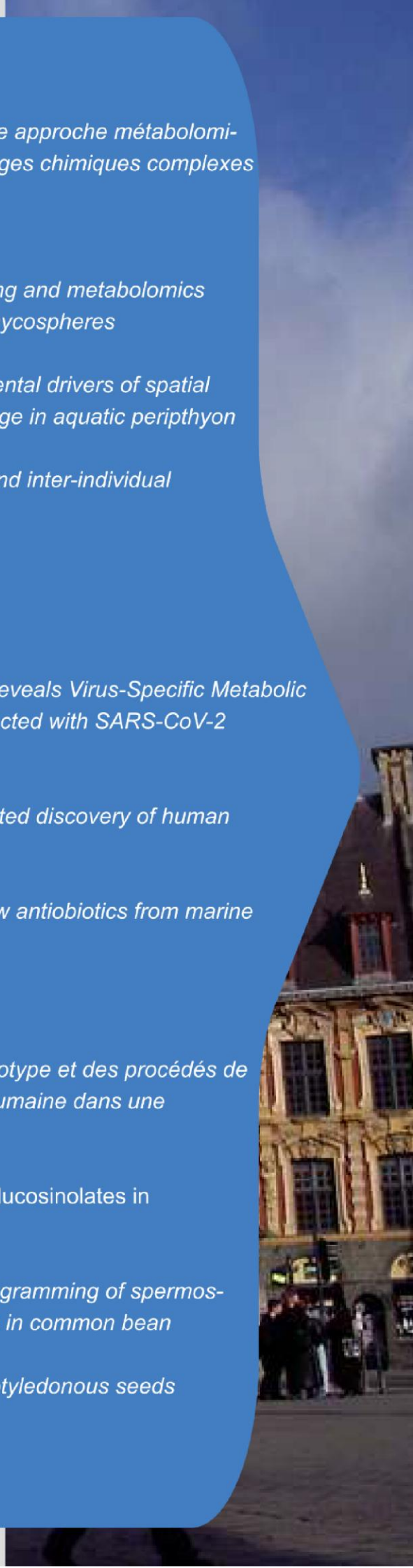
Seeds as ecosystem engineers: metabolomic programming of spermosphere microbial assembly and early-life resilience in common bean

F08 - Theil-Bazingette Mathilde

Comparison study of monocotyledonous and dicotyledonous seeds for their stilbenoid content

17h45 - 18h45 AG RFMF

19h00 - 21h00 Cocktail de bienvenue — Lille Grand Palais



JEUDI 21 MAI 2026

09h00 - 09h45 **Plénière 3 :** Nicole van Dam

Metabolomics for plant and planetary health: Identifying natural plant compounds for crop resistance to insect pests

09h45 - 10h25 **Communications orales**

O10 - Goddard Mary-Lorène

Etude spatio-temporelle de l'interaction Vitis vinifera Neofusicoccum parvum par approches métabolomiques couplées à l'imagerie par spectrométrie de masse

O11 - Falana Nandiyath Achabi

Identification of S-methylcysteine sulfoxide biosynthesis pathways in Brassica species using 13C-fluxomics

10h25 - 10h50 **Pause + Posters**

10h50 - 11h50 **Communications orales**

O12 - Sancharme Mélissa

Uncovering metabolic signatures of abiotic stress and germination in Camelina sativa seeds

O13 - Croutte Antoine

Metabogène : vers un nouvel outil d'annotation pour explorer la diversité biochimique de produits naturels du lin (Linum usitatissimum L.)

O14 - Dupire Francois

Impact of Toasting Temperature and Ethanol Concentration on Oak Wood Extract Composition: A Non-Targeted Metabolomic Analysis Using Ultra-High-Resolution Mass Spectrometry

11h50 - 12h10 **Flashs session 3**

F09 - Peti-Jean Eurydice

Deciphering the vanadium dependent haloperoxidase roles under oxidative stress in a brown alga using knock-out mutants, transcriptomic and metabolomic analyses

F10 - Le Cabec Audrey

Investigating conserved metabolites and associated biosynthetic pathway in seeds: The CoreSeedMet Project

F11 - Fournié Carla

Révéler l'inconnu : Anchor Based Molecular Networking, un outil pour l'identification des Nouveaux Produits de Synthèse

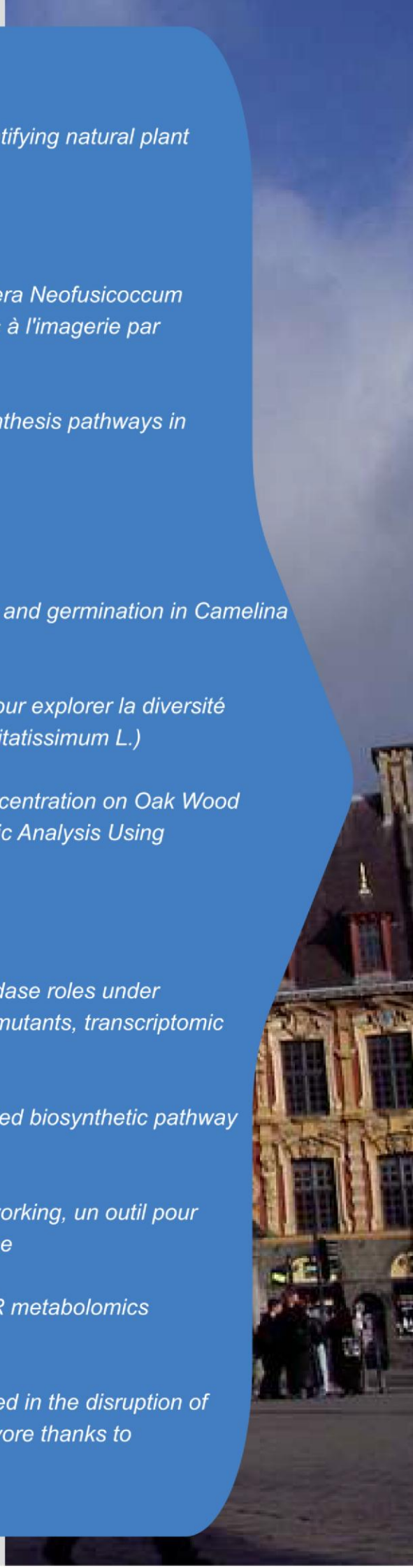
F12 - Gauvreau Julien

Integrated multi-block fast multi-dimensional NMR metabolomics and lipidomics

F13 - Andruszkow Léo

Deciphering mechanisms of service plants involved in the disruption of host plant recognition by a specialist insect herbivore thanks to complementary volatolomic approaches

12h10 - 12h20 SPONSOR SCIEX



12h20 - 14h00 **Repas midi + Posters**

14h00 - 14h45 **Plénière 4 :** Tim Ebbels
Decoding the Metabolome: Intelligence, Integration, and Insight

14h45 - 15h25 **Communications orales**
O15 - Marchand Jérémy
Inter-laboratory evaluation of quantitative 2D 1H NMR for targeted metabolomic analysis of biofluids
O16 - Muller Coralie
Automated mapping of metabolomic compounds onto metabolic networks using MetaNetMap

15h25 - 15h35 SPONSOR AGILENT

15h35 - 16h10 **Pause + Posters**

16h10 - 16h30 **Communications orales**
O17 - Seck Serigne
NMRSCOUT: a dereplication tool integrating multi-dimensional NMR with machine learning

16h30 - 17h00 Membre d'honneur

17h00 - 18h45 Atelier mentorat

19h00 Dîner gala — Palais de la Bourse

VENDREDI 22 MAI 2026

9h00 - 9h45 **Plénière 5** : Manuel Liebeke
Mapping Host-Microbe Metabolic Interactions by Spatial Metabolomics

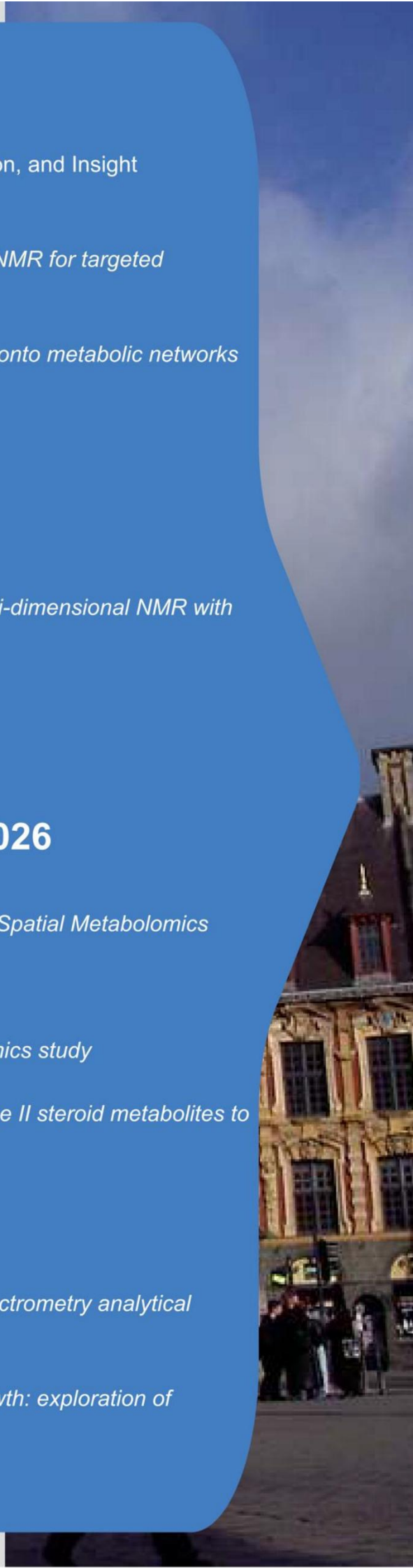
9h45 - 10h25 **Communications orales**
O18 - Schmitz Isabelle
Mass spectrometry imaging for biofilm metabolomics study
O19 - Raux Axel
Comprehensive SPE-LC-HRMS mapping of phase II steroid metabolites to reveal endometriosis complexity

10h25 - 10h45 **Pause + Posters**

10h45 - 11h25 **Communications orales**
O20 - Mangeon Louise
Development of Orbitrap Isotope Ratio Mass Spectrometry analytical workflow for Natural Abundance Fluxomics
O21 - Cahoreau Edern
Microbiota - Host interactions during juvenile growth: exploration of interconnected metabolic networks

11h25 - 11h55 Prix de thèse : Rolin-Portais

12h00 Clôture | À partir de 12h00 Panier repas



Communications des conférenciers invités

Speakers Abstracts

Cédric BERTRAND,

Ingénieur agronome, docteur en Phytochimie, professeur en chimie organique à l'UPVD et directeur du Département de Chimie

Cédric Bertrand est de formation Ingénieur Agronome, professeur de chimie organique à l'Université de Perpignan Via Domitia et spécialiste en métabolomique appliquée aux substances naturelles. Il a développé le concept d'Environmental Metabolic Footprint, qui vise à caractériser les signatures métaboliques laissées par les produits naturels ou de biocontrôle dans l'environnement. Ses recherches en métabolomique non ciblée permettent d'étudier le devenir et l'impact de préparations complexes sur différentes matrices environnementales. Il dirige des travaux au laboratoire CRIOBE - UAR 3278 et coordonne le Laboratoire Vivant AgroLab BioMed, dédiée à l'étude des biosolutions en production végétale.

Le Prof. Cédric Bertrand sera orateur pour la session "One Health – Environnement et exposome".

> Environmental Metabolic Footprinting (EMF) : Une approche métabolomique pour évaluer le devenir et l'impact des mélanges chimiques complexes

Dans l'UE, l'autorisation de mise sur le marché des produits de biocontrôle (ou biopesticide) relève du même cadre réglementaire que celui des pesticides de synthèse. Un obstacle majeur à l'innovation dans ce secteur est l'absence d'outils analytiques permettant d'étudier et de définir la persistance environnementale des extraits naturels complexes utilisés comme substances actives (Amichot, 2025). Bien que des lignes directrices standardisées de l'OCDE existent pour les pesticides de synthèse (qui sont généralement composés d'une seule molécule active), elles ne sont pas adaptées aux mélanges complexes. Pour répondre à ce défi, nous proposons l'Empreinte Métabolique Environnementale EMF (Patil, 2016), un concept innovant basé sur le suivi de l'évolution des profils métabolomiques du sol à l'aide de l'UPLC-HRMS au cours d'études cinétiques en microcosmes (Salvia, 2018). Nous avons développé un workflow analytique complet, incluant des protocoles d'extraction des sols (Ghosson, 2024), des pipelines de traitement des données brutes et des outils bioinformatiques pour introduire une méthode de regroupement des composés en fonction de leurs profils de dégradation spécifiques (Mejait, 2025), conduisant à deux nouveaux indicateurs : le Temps de Dissipation et le Temps de Résilience. De plus l'EMF permet d'étudier l'évolution du méta-métabolome des matrices environnementales c'est-à-dire d'avoir une vision fonctionnelle entre xénométabolome (substances actives et leurs dérivés) et impact sur endométabolome (signature de l'écosystème stressé) et ainsi de dépasser le simple suivi chimique classique et offrir un outil holistique pour caractériser à la fois trajectoire environnementale et empreinte écologique des mélanges complexes.

Timothy M D EBBELS,
Professor of Biomedical Data Science

Le Professeur Tim Ebbels a obtenu son doctorat en 1998 à l'Université de Cambridge. Son groupe se concentre sur l'application de méthodes en bioinformatique, apprentissage automatique et chémométrie aux données post-génomiques, avec un intérêt particulier pour la métabolomique computationnelle.
Ses principaux domaines de recherche incluent le traitement des données RMN et MS, l'intégration et la visualisation des données, l'analyse de réseaux, les séries temporelles et l'annotation des métabolites. Il est notamment connu pour le logiciel BATMAN, conçu pour analyser les spectres RMN métaboliques complexes, ainsi que pour ses travaux récents exploitant les voies biologiques afin de construire des modèles interprétables des données métabolomiques. Tim Ebbels a été directeur de la Metabolomics Society internationale et co-fondateur du London Metabolomics Network. Il a contribué à de nombreuses initiatives visant à améliorer la qualité et la réutilisabilité des données métabolomiques, et siège au comité éditorial de BMC Bioinformatics. Très investi dans la formation, il est directeur du Master of Research (MRes) in Biomedical Research à l'Imperial College (plus de 1000 étudiants formés) et responsable du cours spécialisé Data Analysis in Metabolomics. Il est Fellow de la Royal Society of Chemistry et membre honoraire à vie de la Metabolomics Society.

> Decoding the metabolome: intelligence, integration, and insight

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Metabolomics datasets are inherently complex, capturing rich and multidimensional information on an organism's biochemical state. However, this complexity presents a major challenge: extracting robust, biological insight from high-dimensional, heterogeneous and noisy data. As a result, computational approaches are increasingly central to the field, enabling the transformation of analytical measurements into biological understanding.

In this lecture, I will provide an overview of computational metabolomics research at Imperial College London, focusing on strategies that integrate data, enhance interpretability, and improve analytical outputs. Key themes will include the development of pathway-based models to support biologically meaningful interpretation, approaches for multimodal data integration across analytical platforms and omics layers, and the application of artificial intelligence to enhance data quality and extraction of information.

I will highlight recent advances from our group, including pathway-driven integrative models that leverage modest but coordinated signals across datasets to reveal underlying biology, and deep learning methods for resolution enhancement in J-resolved NMR spectroscopy. These approaches demonstrate how computational approaches can both improve data quality at the analytical level and enable more interpretable, mechanism-oriented analysis at the systems level.

Overall, I hope to convey how the combination of (artificial) "intelligence, integration, and insight" are positioning computation as a key driver of discovery in metabolomics science.

Manuel LIEBEKE,
Professor of Metabolomics at the Institute of Human Nutrition and Food Sciences, Faculty of Agricultural and Nutritional Sciences, Kiel University

Manuel Liebeke est chercheur spécialisé en métabolomique et en interactions métaboliques. Depuis 2024, il occupe la Chaire d'excellence du Schleswig-Holstein (SH-Chair) à l'Université de Kiel. Auparavant, il a été nommé professeur de métabolomique à l'Université de Kiel (CAU), où il dirige également un groupe passerelle entre l'Institut Max Planck de microbiologie marine et la CAU. Son parcours académique est marqué par des contributions majeures visant à identifier de nouveaux rôles des métabolites dans les interactions microbiennes et animales. En 2021–2022, Manuel Liebeke a été professeur invité à la DTU de Copenhague (Centre d'excellence : Microbial Secondary Metabolites), un poste attribué par la Fondation Otto Monstedt. Depuis 2018, il dirige le groupe de recherche indépendant sur les interactions métaboliques à l'Institut Max Planck de microbiologie marine, au sein du département Symbiosis. Plus tôt dans sa carrière, il a travaillé comme chargé de recherche à l'Institut Max Planck de microbiologie marine ainsi qu'à l'Imperial College London. Il a obtenu un doctorat en biologie pharmaceutique à l'Université de Greifswald en 2010.

> Mapping host-microbe metabolic interactions by spatial metabolomics

Metabolism in multicellular organisms is not confined to host cells alone but emerges from continuous biochemical interactions with resident microbes. These host–microbe metabolic exchanges are spatially organized across tissues and microenvironments, yet most metabolomics approaches using bulk measurements obscure where metabolic transformations occur and who performs them.

Here, I present a spatial metabolomics framework to investigate host–microbe metabolic interactions in situ. By combining mass spectrometry–based metabolomics with spatially resolved sampling and multimodal imaging strategies, we map metabolites across host tissues colonized by microbes. This approach enables the direct localization of microbially derived metabolites, host metabolic responses, and shared metabolic intermediates at relevant spatial scales.

Using representative host–microbe systems, we demonstrate that spatial context is essential for interpreting metabolic phenotypes. Metabolite distributions reveal localized metabolic activities that are invisible in homogenized samples, including gradients of microbial metabolites at host interfaces and region-specific host metabolic adaptations. These spatial patterns provide mechanistic insight into how microbial metabolism reshapes host biochemical networks beyond what relative abundance measurements alone can capture.
Our results highlight spatial metabolomics as a critical tool for dissecting host–microbe metabolism and for bridging the gap between microbial community composition and functional metabolic output. By resolving where metabolites are produced, transformed, and accumulated, mass spectrometry gains the ability to move from descriptive microbiome studies toward a spatially informed, mechanistic understanding of metabolism in complex biological systems.

Nicole VAN DAM,
Scientific Director Leibniz IGZ/Full Professor Plant-Biotic Interactions FSU Jena

Nicole M. van Dam est une écologue qui cherche à comprendre les mécanismes moléculaires et chimiques à la base des interactions des plantes. Elle est professeure titulaire à l'Université Friedrich Schiller de Léna (Allemagne) et directrice scientifique du Leibniz Institute of Vegetable and Ornamental Crops (IGZ) à Großbeeren, en Allemagne, depuis 2022. Ses recherches impliquent des approches métabolomiques et transcriptomiques pour étudier la façon dont les plantes réagissent aux herbivores, à la fois au-dessus et au-dessous du sol. Dans ce cadre, elle s'intéresse particulièrement à la compréhension de la manière dont l'énorme diversité chimique observée chez les plantes est apparue et est maintenue par la sélection naturelle. Les résultats de ses recherches ont des implications pour la théorie écologique et l'agriculture durable, notamment dans l'élaboration de stratégies de protection intégrée des cultures.

Le Prof. Nicole van Dam sera oratrice pour la session "One Health – Plantes".

> Metabolomics for plant and planetary health: Identifying natural plant compounds for crop resistance to insect pests

Plants have been able to survive herbivory for millions of years without pesticides. To do so, they have evolved a dazzling diversity of morphological and chemical defenses to deter or to kill herbivores. Untargeted metabolomic analyses have shown that any plant may produce thousands of specialized metabolites with functions in direct and indirect plant defense. Breeders may use this information as leads for selecting crops that are more resistant and less reliant on pesticides. Here, I will show how we applied untargeted metabolomics to identify novel strategies to identify oilseed rape (OSR: Brassica napus) accessions that are more resistant to larvae of the cabbage root fly (Delia radicum). By performing untargeted LC-MS based metabolomics of 45 OSR accessions and testing subsets thereof in insect behavioral and performance assays, we could identify several metabolites that may contribute to reduced feeding preference and performance of this root pest. Using mutant lines and additional transcriptional analyses we are currently testing whether specific metabolites indeed are linked to increased resistance. In the end, the knowledge gained by this eco-metabolomics approach will be linked to genomic information as a basis for generating root fly resistant OSR varieties.

Lynn VANHAECKE,

PhD, Professor and Principal investigator of the Integrative Metabolomics Laboratory at Ghent University (Belgium)

Lynn Vanhaecke est professeure titulaire et responsable du Laboratoire de Métabolomique Intégrative à l'Université de Gand (Belgique) depuis 2011. Elle occupe également un poste à 20 % à l'Institut de Sécurité Alimentaire Mondiale de la Queen's University Belfast (Royaume-Uni) depuis 2018. Ses principaux objectifs de recherche portent sur l'analyse holistique des petites molécules par métabolomique et lipidomique, utilisant la spectrométrie de masse à haute résolution (notamment l'ionisation ambiante), dans le cadre de l'axe alimentation–microbiome–santé. En 2023, elle a obtenu une bourse ERC Consolidator pour poursuivre ses travaux visant à faire progresser la métabolomique vers la médecine de précision pédiatrique.

Lynn est membre active du conseil d'administration de la Nutritional Genomics Society et membre élue du conseil de la Metabolomics Society.

Le Prof. Lynn Vanhaecke sera oratrice pour la session "One Health – Hommes".

> From gastrointestinal metabolomics to pediatric precision medi cine through source-based metabotyping

Metabolomics is rich in promise yet still relatively slow, complex and costly for routine clinical use. At the Laboratory of Integrative Metabolomics (LIMET) within ERC Consolidator Grant MeMoSA, we address this gap by advancing gastrointestinal metabolomics toward a source-based and clinically actionable framework for pediatric precision medicine. Focusing on non-invasive stool and saliva sampling, we combine comprehensive dual-UHPLC-HRMS/MS metabolomics and lipidomics with rapid ambient ionization mass spectrometry workflows based on MetaSAMP® and LA-REIMS, thereby linking deep molecular annotation to scalable, real-time metabotyping. Building on deeply phenotyped pediatric cohorts (ca. 1500 children), we integrate metabolome and lipidome data with anthropometric, diet, microbiome, lifestyle, medication, psychosocial and clinical parameters to model how specific sources shape metabolic phenotypes associated with pediatric overweight and obesity. In parallel, in vitro digestion, in vivo murine models and in silico approaches will be used to strengthen causal interpretation of source-metabolite relationships. After the first two years, MeMoSA has established its conceptual and technological backbone: 1. automated large-scale simultaneous extraction of fecal metabolome and lipidome, 2. advanced dual UHPLC-HRMS(/MS) metabolomics/lipidomics workflows for biofluids, 3. annotation-oriented ambient metabolomics strategies using cyclic ion mobility in hyphenation with LA-REIMS for biofluids, and 4. the data infrastructure needed for source-based prediction from automated targeted over untargeted preprocessing incl. normalisation, correlation, and ML-based analysis. Together, these efforts aim to move metabolomics beyond descriptive biomarker discovery toward mechanistic insight, longitudinal monitoring, and personalized interventions in children at cardiometabolic risk.

Communications orales

Oral 1 – O 01

Xtremomics ou exploration métabolomique de l'adaptation humaine aux environnements extrêmes

Jean-Charles Martin[1,2], Audrey Bergouignan[3], Samuel Vergès[4], David Martin[2], Stéphane Nottin[5], Caroline Le Goff[6], François Guerrero[7], Nicolas Vallée[8,9], Céline Ramdani[9], Catherine Tardivel[10,11], and Grégoire Millet[12]

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[11] Aix-Marseille Université - C2VN – Aix-Marseille Université - Faculté des Arts, Lettres, Langues et Sciences Humaines – France
[12] Université de Genève = University of Geneva – Suisse

L'organisme humain possède une remarquable plasticité d'adaptation aux variations de son environnement. Toutefois, l'exposition aux conditions extrêmes constitue un défi majeur pour les capacités d'ajustement biologique. Notre objectif est d'identifier des systèmes métaboliques universels capables de soutenir la résilience de l'organisme face à des environnements extrêmes. Pour cela, nous avons réalisé l'analyse LC/MS du plasma et/ou urines de sujets humains placés en conditions d'hypoxie chronique liés à l'altitude (5300m), de plongeurs en séjour de plusieurs jours en capsule sous-marines sous atmosphère d'héliox (30%O_2/70% He), de volontaires immobilisés pendant 2 mois en position couchée mimant les séjours spatiaux, de militaires en opération, d'ultra-marathonien en haute montagne (370km course). Environ > 200 à 400 métabolites ont été annotés et stratifiés en unités fonctionnelles. Ces unités sont déclinables en amont en voies biochimiques et en aval en modules du système biologique. Cette représentation normalisée des systèmes métaboliques permet un comparatif non biaisé des différentes situations.

Notre modélisation met en évidence un nombre restreint de patrons métaboliques communs à l'ensemble des situations étudiées. Il s'agit : (i) du métabolisme du tryptophane et des indoles, en interaction étroite avec le microbiote et le métabolisme primaire de l'hôte ; (ii) des systèmes de défense cellulaire intégrant les voies du glutathion, de la sérine/ thréonine/glycine et de la caféine ; et (iii) des adaptations du système cardiovasculaire, également associées au métabolisme de la caféine.

Il semble qu'un patron métabolique de " rescue outcome pathway " générique s'active pour contribuer à l'adaptation aux conditions extrêmes afin d'assurer la survie.

Oral 2 – O 02

Multiblock Chemometric Approaches to Decode Multisource Molecular Signatures of Perceived Stress in Healthcare Students

Célie Da Silva[1,2], Mathieu Galmiche[1,2], Oriane Strassel[1,2], Sergey Girel[1,2], Isabel Meister[1,2], Zeïneb Zghal[1,2,3,4,] Sabrina Pagano[3,4], Nicolas Vuilleumier[3,4], Camille Piguet[5,6], Françoise Jermann[7], Julien Boccard[1,2], and Serge Rudaz[1,2]

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High stress and mental strain are prevalent among healthcare students and persist through-out clinical careers, impairing empathy and quality of care. Mindfulness-Based Cognitive Therapy for Life (MBCT-L) has shown promise in reducing stress. However, the underlying biological mechanisms of these effects remain unclear. This work presents initial findings of the e-SMILE project, an extensive metabolomics study evaluating the potential of MBCT-L to reduce stress and improve well-being of healthcare students. Multisource data were collected from blood samples using untargeted and targeted LC-MS approaches. Three metabolomics blocks were measured, including 1,147 lipids and 425 metabolites (Level 1 and 2 annotations) from untargeted profiling, and 86 targeted steroids recoded into 148 pathway-based ratios to enhance biological interpretability. A fourth block comprising 32 inflammatory and immune markers measured by electrochemiluminescence immunoassay (ECLIA) was collected. These data were investigated alongside clinical scores, and particularly the Perceived Stress Scale (PSS) used as a continuous outcome variable. Individual block-specific OPLS models showed low explanatory and predictive performance. In contrast, an integrative analysis considering all blocks simultaneously via the Consensus OPLS multiblock method achieved strong explanatory power and validated predictivity. The block involving metabolites contributed most strongly to the predictive component, while lipids, steroid ratios, and immune markers provided complementary biological information, reflecting the distributed molecular signature of stress. Key associations included serotonin, tyrosine, acyl-carnitines, ether-phosphatidylethanolamines, and sphingomyelins. Steroid ratios revealed also a strong biological sex effect, underscoring the need to explicitly account for sex as a confounding factor using mixed-effects or variance decomposition strategies.

Oral 3 – O 03

Integration of Heterogeneous Biochemical Knowledge and Assembly of the Next Reconstruction of Human Metabolism with a Focus on Lipids

Marco Pagni[1]

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The development of ReconX, the next-generation reconstruction of human metabolism, requires precise integration of biochemical knowledge from diverse resources. Foundational information is derived from earlier metabolic reconstructions (Recon3, VMH), which support constraint-based modelling. Additional annotations are incorporated from public ontologies such as ChEBI and RHEA, as well as the SwissProt knowledgebase. Because each resource uses distinct identifier namespaces, robust cross-resource alignment is essential. Metabolite reconciliation is performed using a tailored MetaNetX workflow, while gene and protein harmonization relies on SwissProt.

A major challenge lies in the incomplete representation of lipids in existing models, where lipid species are often encoded as generic compounds with undefined R-groups. To overcome this limitation, we aim to computationally enumerate a comprehensive network of all theoretically possible human lipids and their associated reactions, transitioning from generic lipid pools to a fully atom-resolved lipid map. SwissLipids provides the primary reference for lipid structures. High-fidelity fluxomics modelling requires bridging MetaNetX-based reconciliation with the chemical ontology of ChEBI, the enzymatic reaction knowledge of RHEA, and the lipid-specific information of SwissLipids.

Integration, validation, and downstream use of these heterogeneous data sources occur within a knowledge graph, ReconXKG, implemented in RDF/SPARQL and managed by in-house software. This multidisciplinary effort presents both technical and collaborative challenges. It is carried out within Recon4IMD, a European initiative developing a diagnostic tool for Inherited Metabolic Diseases through the integration of metabolomics, genomics, and metabolic modelling.

Oral 4 – O 04

Integrating metagenome-scale metabolic modelling and metabolomics to identify metabolic interactions in *Microcystis* phycospheres

Juliette Audemard[1,2], Nicolas Creusot[3], Julie Leloup[4], Charlotte Duval[5], Sébastien Halary[5], Lou Mary[5], Melissa Eon[3], Thomas Forjonel[3], Mohamed Mouffok[2], Puppo Rémy[5], Elodie Belmonte[6], Véronique Gautier[6], Jeanne Got[7], Marie Lefebvre[2], Gabriel Markov[8], Coralie Muller[1], Benjamin Marie[5], Clémence Frioux[1], and **Binta Diémé**[2]

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Deciphering how microbial interactions shape functional outcomes in natural communities remains a central challenge in microbial ecology. In freshwater blooms, cyanobacterial phycospheres are highly dynamic microscale habitats, yet the metabolic interactions structuring their functional organization remain poorly understood. Microcystis, one of the most widespread cyanobacterial genera, develops within a phycosphere where specialized interactions with its microbiome are thought to influence bloom formation and toxicity. Here, we combined metagenomics, metabolomics, and genome-scale metabolic modeling to characterize metabolic interactions within and across twelve reduced, cultivated Microcystis phycospheres originating from a single bloom event. Using complementary extraction protocols to maximize metabolome coverage and annotation, metabolomic analyses revealed concordant specialized metabolic profiles among Microcystis genotypes and clear differences between genospecies. At the community level, meta-metabolome variation was largely driven by cyanobacterial metabolic outputs.

The distribution of metabolic reactions within Microcystis aligned with genospecies boundaries, whereas community-level metabolic landscapes diverged from cyanobacterial phylogeny, indicating functional decoupling between cyanobacteria and their associated microbiomes. Metabolic modeling, together with the identification of toxic specialized metabolites, further highlighted differences in metabolic potential among phycospheres. Our modelling also revealed extensive functional complementarity within and between phycospheres, enabling collective access to metabolic capabilities that are unreachable by individual community members alone. Overall, we demonstrate that phycosphere metabolism is strongly shaped by Microcystis genospecies, revealing a clear genotype–chemotype relationship. These findings advance our understanding of Microcystis phycosphere functioning, illustrate the relavance of multi-omics systems biology approaches, and underscore the ecological importance of interspecies and inter-phycosphere metabolic interactions in structuring bloom-associated microbiomes.

Oral 5 – O 05

Predictive metametabolomics unravels environmental drivers of spatial heterogeneity of microbial metabolome assemblage in aquatic peripthyon

Mariana Pinheiro-Costa-Pimentel[1,2], Amelie Malherbe[1,2], Mélissa Eon[1], Chloé Bonnineau[1], Sébastien Boutry[1], David Carayon[1], Rémy Cordazzo[2,3], Claudia Rouveyrol[2,3], Cédric Cassan[2,3], Pierre Pétriacq[2,3], Sylvain Prigent[2,3] , Nicolas Creusot[1,2]

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Facing global change, microbial periphytic communities are increasingly used in ecotoxicology to assess how chemical contamination impacts freshwater ecosystems. While laboratory studies have clarified periphyton responses to pollutants, they do not capture the complexity of natural environmental variability. This limits our ability to distinguish chemical effects from background ecological influences in the field. Metabolomics offers a comprehensive, functional snapshot of community-wide microbial activity under real conditions. Combined with machine learning to integrate metabolomic and environmental data, it enables identification of key drivers of metametabolome variability. This study therefore aims to assess how in situ environmental factors, structure the spatial heterogeneity of the periphyton metametabolome trough the implementation of a predictive meta-metabolomics framework. To do so, autochthonous periphyton was sampled from 100 rivers across France, selected to represent a broad gradient of physico-chemical properties and ecological status based on national water agency data. At each site, photosynthetic yield was measured in situ alongside comprehensive water quality parameters, including micropollutants, nutrients, pH, and temperature. Global biomass indicators (e.g., proteins, starch) and LC-HRMS-based untargeted metabolomics analyses were further implemented. The diversity of physico-chemical profiles confirmed the suitability of the sites to capture strong environmental contrasts. Machine learning enabled the identification of several features predictive of environmental parameters (e.g. pesticide concentration). Subsequent metabolite and pathway annotation are on going to elucidate microbial metabolic adaptations. Overall this study will support biomarker discovery for chemical stress, and define the normal operating range of the periphyton metametabolome for improved biomonitoring.

Oral 6 – O 06

One-year longitudinal follow-up to assess intra- and inter-individual metabolite variations in healthy volunteers

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In healthcare, most metabolomics studies focus on pathologies by studying inter-individual and/or inter-group variations in metabolite concentrations. However, with patient care shifting toward a more personalized approach, integrating metabolomics requires understanding normal intra-individual variations to detect pathological deviations. Currently, these ”normal” variations remain poorly characterized, making it essential to study the metabolome of healthy individuals over time.

For this purpose, we conducted a one-year longitudinal study involving 30 healthy volunteers. Serum was collected weekly for ten weeks and then monthly for ten months, following European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group on Biological Variation recommendations. Questionnaires were also completed at each visit to report habit changes and lifestyle events potentially affecting the metabolome.

As quantification is required, NMR appeared as the most suitable analytical tool. Over the ten-week period, 41 metabolites were classified based on their intra-individual variability, from the least to the most fluctuating. A similar pattern emerged from monthly samples, confirming variability consistency over time. Additionally, we applied the Metabolomic Informative Content (MIC) approach to stratify individuals based on their metabolome variation. Finally, using questionnaire data, linear mixed models identified which events induced significant longitudinal differences at the individual level.

Our results enable the stratification of blood metabolites according to their short- and long-term within-subject variability. Moreover, questionnaire analyses revealed that several lifestyle events significantly modify the metabolome, meaning such factors must be considered when interpreting metabolomics data. Together, these results represent a key step toward integrating reliable metabolomics profiling into routine clinical practice.

Oral 7 – O 07

Comparative Untargeted Metabolomic Profiling Reveals Virus-Specific Metabolic Reprogramming in Human Airway Epithelium Infected with SARS-CoV-2 and Influenza A Virus

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Influenza A virus (IAV) are major respiratory pathogens responsible for global pandemics and epidemics outbreaks. While both viruses alter host cellular metabolism (Ayres 2020, Bahadoran 2020, Rubayet Hasan 2021), direct comparative studies are lacking, limiting the identification of virus-specific metabolic signatures. Here, we performed a comparative analysis of metabolic reprogramming induced by SARS-CoV-2 and IAV in a reconstituted human airway epithelium (HAE) model using an untargeted LC–MS/MS metabolomics approach.

HAE cultures were infected with SARS-CoV-2 or IAV and monitored from 24 to 96 hours post-infection. Infection dynamics were characterized by transepithelial electrical resistance, IL-6 secretion, viral replication, and transmission electron microscopy. These phenotypic parameters were integrated into a clustering strategy to classify samples according to infection progression. Endometabolome was profiled using Orbitrap-based high-resolution mass spectrometry. Data processing included feature detection with MZmine, filtering, QRILC-based missing value imputation, normalization in R, and metabolite annotation through GNPS, Compound Discoverer, and an in-house spectral database.

Phenotype acquisition assesses for effective infections and their progression with infection time. Unsupervised multivariate analyses discriminated non-infected, SARS-CoV-2-, and IAV-infected samples, revealing distinct metabolic signatures. Supervised modeling identified shared inflammatory-associated metabolites, including kynurenine, formylkynurenine, inosine, betaine, and platelet-activating factor. Notably, SARS-CoV-2 infection specifically induced ophthalmate accumulation, a glutathione-related metabolite associated with oxidative stress and mitochondrial dysfunction.

Together, these results highlight the robustness of the HAE–metabolomics platform for distinguishing virus-specific metabolic responses and identifying candidate biomarkers, with ophthalmate emerging as a potential marker of SARS-CoV-2 infection and disease severity.

Oral 8 – O 08

Simultaneous targeted quantification and untargeted discovery of human serum metabolome: SQUAD Metabolomics

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We report a novel metabolomics workflow, based on a SQUAD (Simultaneous Quantification And Discovery) approach, enabling concurrent targeted quantification and untargeted profiling of the human plasma metabolome. The method employs a four-injection high-performance liquid chromatography – mass spectrometry (LC–MS) sequence combining reversed-phase (RP) and hydrophilic interaction (HILIC) separations in positive and negative electrospray ionisation modes.

Using a Thermo IQ-X Tribrid mass spectrometer, SQUAD quantitatively and sensitively targets 150 known metabolites via the linear ion trap with calibration curves while simultaneously acquiring high-resolution full-scan (MS^1) and data-dependent MS/MS spectra for untargeted analysis via the orbitrap mass analyser. All 250 metabolites exhibit linear responses (typically $R2 > 0.99$) across wide concentration ranges with low limits of detection, enabled by the incorporation of native standards and selected stable-isotope internal standards. The method is validated for precision, accuracy, and matrix effects following standard guidelines.

We are currently applying this pipeline to a kidney transplant patient (KTX) cohort (IMMEDIATE EU-funded project). While transplantation transforms survival in end-stage renal disease, early signs of subclinical graft dysfunction are often missed by conventional markers. We aim to provide earlier, systems-level insight by capturing dynamic biochemical changes. By evaluating KTX samples, we aim to obtain absolute concentrations for a curated biomarker panel alongside broad untargeted profile. We are integrating these targeted and untargeted layers with clinical endpoints, including graft function, rejection episodes, and immunosuppressant exposure. Ultimately, this analysis will define robust metabolic signatures for early graft injury and outcome prediction, helping to discover and validate rejection-risk and patient-response markers.

Oral 9 – O 09

Eco-inspired multicultures for the discovery of new antiobiotics from marine fungi

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Antimicrobial resistance constitutes a major public health issue, requiring the development of new therapeutic molecules. Marine fungi and their specialized metabolites (SMs) represent an underexploited source of potential antibiotics. However, under conventional laboratory conditions the number of observed SMs remains limited relative to their biosynthetic capabilities. To induce the expression of cryptic pathways in strains from marine holobionts, the use of host-derived culture media and co-cultures of microbial partners are some of the most promising strategies even if little employed. However, co-culture methods are mainly performed using pairs of microorganisms, which does not reflect what naturally occurs within marine microbiomes. This project aspires to develop eco-inspired multicultures of different fungal strains sampled from the seaweed Palmaria palmata, aiming to highlight metabolic inductions in microbial consortia when cultured on a reconstituted seaweed-based medium. Four fungal strains belonging to the genera *Penicillium*, *Aspergillus*, *Acremonium*, and *Parengyodontium* were cultivated on 12 different culture media including *P. palmata* host-derived. Extracts obtained were tested for antibacterial activities and analyzed by UHPLC-HRMS/MS to construct bioactive molecular networks. This allowed to find a "gold-standard" host-derived medium which has then been employed for multi-cultures involving 2 to 4 of the strains. MS-based chemometrics analyses led to highlight the induction of specific signals in some of the microbial consortia. One promising microbial consortium has been scaled-up in order to isolate the most promising and original compounds. This study lays the foundations for a new concept in fungal NPs discovery combining multicultures with the use of eco-inspired host-derived media.

Oral 10 – O 10

Étude spatio-temporelle de l'interaction Vitis vinifera – Neofusicoccum parvum par approches métabolomiques couplées à l'imagerie par spectrométrie de masse

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La vigne est aujourd'hui confrontée à une intensification des stress biotiques et abiotiques. Dans un contexte de réchauffement climatique, les maladies de dépérissement, notamment les dépérissements liés aux Botryosphaeriaceae, apparaissent de plus en plus fréquemment, avec des conséquences croissantes pouvant aller jusqu'à la mort des ceps.

Pour décrypter les mécanismes d'infection fongique et les réponses de défense de la plante, nous avons mis en place des études spatio-temporelles sur des entre-nœuds détachés issus de différentes sous-espèces de Vitis vinifera infectés par Neofusicoccum parvum, l'un des champignons les plus fréquemment isolés et les plus virulents de la famille des Botryosphaeriaceae. Ces travaux révèlent non seulement des différences marquées de tolérance entre sous-espèces, mais mettent également en évidence une reprogrammation du métabolisme primaire. L'analyse d'extraits aqueux par GC-MS a montré des modifications métaboliques significatives, tandis que l'imagerie par spectrométrie de masse (MSI) a permis d'identifier des phénomènes de relocalisation et des distributions spécifiques de métabolites au sein des coupes de sarments.

Par ailleurs, l'étude du métabolisme spécialisé à partir d'extraits méthanoliques analysés en LC-MS/MS confirme et approfondit nos résultats préliminaires publiés dans Metabolites (Labois et al. Metabolites 2020, 10, 232-251 DOI: 10.3390/metabo10060232). Elle souligne le rôle central de stilbènes spécifiques dans les mécanismes de défense de la vigne, mettant en lumière leur rôle clé dans la résistance aux pathogènes.

Oral 11 – O 11

Identification of S-methylcysteine sulfoxide biosynthesis pathways in *Brassica* species using ^{13}C-fluxomics

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Rapeseed (*Brassica napus*) is a major oilseed crop in Europe, but its yield potential is threatened by the need the reduce the use of pesticides in a context of agroecological transition of crop system. The manipulation of natural defence mechanisms against pests is therefore seen as a promising target for crop improvement. Brassica species are known to produce volatile sulfur-containing compounds that can modulate pest attraction/repulsion. One the most abundant precursors of these volatile compounds is S-methyl-L-cysteine sulfoxide (SMCSO). Recent results showed that this non-proteinogenic amino acid can itself mediate a deterrent effect against some pests. Despite its biological importance, SMCSO biosynthesis remain unclear and could proceed through either the serine pathway, the glutathione pathway or a direct S-methylation of cysteine. In order to identify the metabolic origin of SMCSO in *B. napus*, we traced the fate of ^{13}C-labelled precursors within SMCSO metabolism in both leaf and root tissues along a kinetic under light and dark conditions. Isotopic analyses with a UPLC-TQD system provided evidences at the isotopologue level for the existence of the serine and the glutathione pathway. The implication of the photorespiratory pathway in SMCSO biosynthesis was also observed based on the light-dependence of SMCSO ^{13}C-enrichment when using ^{13}C3-serine as a probe. Targeted inhibition of key enzymes associated to the serine and glutathione pathways further allowed to evaluate their respective contribution of the total pool of SCMSO. The generated results will help to identify the genes encoding each pathway and to understand their evolutionary history among *Brassica* species.

Oral 12 – O 12

Uncovering metabolic signatures of abiotic stress and germination in *Camelina sativa* seeds

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Camelina (*Camelina sativa*) is an oilseed crop of increasing interest due to the high nutritional quality of its oil and its strong resilience to environmental constraints. Conducted within the framework of the GERMOLEOPRO project, our study combined physiological analyses with metabolomic, proteomic, and peptidomic approaches to assess the impact of environmental stresses and germination on the metabolic composition of camelina seeds. This work contributes to optimizing seed nutritional value and reducing antinutritional compounds through germination, in the context of the transition toward sustainable, plant-based protein sources.

LC-MS/MS-based metabolomic and proteomic analyses were performed on seeds of the camelina genotype "Céline" obtained from plants subjected to water stress (WS), heat stress (HS), combined WS x HS, or optimal conditions. These analyses were conducted on both germinated and non-germinated seeds to assess the role of germination in shaping seed composition.

Untargeted metabolomic analyses revealed a wide diversity of polar metabolites and highlighted clear effects of environmental stresses and germination on the metabolic composition of camelina seeds. The detected metabolome included several major classes: glucosinolates, flavonoids, phenolic compounds, amino acids, and carbohydrates. These metabolite profiles were organized according to stress conditions and germination status. Complementary proteomic and physiological analyses supported these findings and indicated consistent effects of stress and germination on seed molecular profiles and functional traits. Together, these integrated physiological, metabolomic, and proteomic approaches provide a comprehensive understanding of how abiotic stresses and germination shape camelina seed composition and quality, and support the identification of leverage points for improving nutritional traits.

Oral 13 – O 13

Metabogène : vers un nouvel outil d'annotation pour explorer la diversité biochimique de produits naturels du lin (*Linum usitatissimum* L.)

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Les plantes constituent une source majeure de molécules bioactives, produisant une grande diversité de composés aux propriétés chimiques et biologiques variées. Toutefois, leur identification reste longue en raison des étapes de fractionnement bioguidé nécessaires avant une caractérisation complète par résonance magnétique nucléaire (RMN) et spectrométrie de masse haute résolution (HRMS).

Dans ce contexte, nous développons une preuve de concept d'un outil d'annotation innovant combinant données analytiques (LC-HRMS) et approches génomiques de type mQTL afin d'accélérer l'identification des métabolites. Des travaux récents menés au sein de l'UMRT BioEcoAgro INRAE 1158 ont mis en évidence, chez le lin (*Linum usitatissimum* L.), des corrélations entre marqueurs génétiques et accumulation de métabolites structurellement proches. A partir d'une population de lignées recombinantes (RILs) issue du croisement entre un lin d'hiver et un lin de printemps, nous avons regroupé des métabolites partageant à la fois des régions génomiques communes et des similarités structurales avec un niveau de précision inédit. L'approche permet notamment de distinguer les flavones di-glycosides dérivées de l'apigénine de celles issues de la lutéoline, démontrant ainsi la capacité du modèle à discriminer des composés ne différant que par leur aglycone. Elle différencie également les flavones selon leurs modifications (méthylation, glycosylation) et selon la nature et la position des résidus glycosidiques (O- ou C -). Au-delà des flavones, des regroupements spécifiques ont été observés pour les cyanogènes, lignanes et dérivés d'acides hydroxycinnamiques.

En cours d'optimisation, ce modèle d'annotation contribuera à accélérer l'exploration du métabolome du lin et à terme orienter l'élucidation des voies de biosynthèse.

Oral 14 – O 14

Impact of Toasting Temperature and Ethanol Concentration on Oak Wood Extract Composition: A Non-Targeted Metabolomic Analysis Using Ultra-High-Resolution Mass Spectrometry

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The organoleptic profile of barrel-aged-wine is strongly influenced by the compounds resulting from wood toasting, a process consisting in heating the staves at different temperatures during cask production. If several studies have investigated the toasting influence on the molecular composition of the wine, researches on the wood material, in the context of vinification, are less represented. Here, model toasted and untoasted oak samples were used to assess the effect of the toasting temperature and ethanol concentration, on the molecular composition of the hydroalcoholic extracts from wood maceration.

Oak pieces toasted at different temperatures (from 140 to 200 ◦C) and untoasted wood samples were macerated in five different hydroalcoholic solutions (ethanol concentrations ranging from 0 to 100%). The resulting extracts were analyzed by ultra-high-resolution mass spectrometry (UHRMS) coupled with electrospray ionization (ESI) or atmospheric pressure photoionisation (APPI).

More than 10,000 distinct molecular formulae were obtained by UHRMS, highlighting the molecular complexity of these samples. The influence of both toasting temperature and ethanol concentration, on the wood extract molecular composition, was also evidenced. Signals corresponding to carbohydrate-derived species decreased with increasing ethanol content, but were more intense for lower toasting temperatures. Furthermore, the relative abundance of ellagic acid, an oak wood marker, increased with ethanol concentration. Vanillic acid, associated with creamy and vanilla notes, was putatively identified in samples subject to high toasting temperature. APPI allowed to detect 800 exclusive compounds, including putative jasmone and 4-vinylguaiacol, which respectively impart woody, herbal, and floral aromas, and clove and roasted almonds notes.

Oral 15 – O 15

Inter-laboratory evaluation of quantitative 2D ^{1}H NMR for targeted metabolomic analysis of biofluids

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While targeted quantitation of metabolites in biofluids is usually performed using 1D ^{1}H NMR, this technique is often hampered by signal overlap. To overcome this issue, fast quantitative 2D NMR methods have been developed. However, these methods lack standardization and remain used by a limited number of expert groups. Hence, to confirm the ability of fast 2D NMR to provide accurate metabolite concentrations and extend its use, we present the first inter-laboratory ring test based on fast quantitative 2D ^{1}H NMR. 1H homonuclear 2D NUS ZF-TOCSY experiments were implemented and standardized from acquisition to 2D spectra processing and quantitation on five NMR spectrometers throughout the French territory from the MetaboHUB infrastructure. Absolute quantitation of 34 urinary metabolites within an interlaboratory ring-test was then performed using external calibration, involving five acquisition sites and twelve operators for processing.
Across all acquisition sites and operators, a mean trueness < 5% was obtained for 31 metabolites and a mean precision < 5% for 29 of them. Comparatively, similar performance was obtained from our previous study on 1D ^{1}H NMR although the latter only focused on interoperator processing variability. Here, the fast 2D approach was also applied to a real-case study to quantify these metabolites in a real-case study associated with Cushing syndrome. These results demonstrate that, if standardized, fast 2D-NMR can be implemented for quantitative metabolomic studies of biofluids, even including various platforms, configurations and operators while providing accurate metabolite concentrations. This enables the future application of such approach for large-scale studies involving multiple partners.

Oral 16 – O 16

Automated mapping of metabolomic compounds onto metabolic networks using MetaNetMap

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Understanding biological systems requires integrative and multi-level approaches. Genome Scale Metabolic Networks (GSMNs), that are derived from genome annotation, capture the metabolic capabilities of an organism. In contrast, metabolomics gives an insight into what is really happening in an organism under specific conditions. Mapping molecules identified from metabolomic experiments onto GSMNs offers several advantages: mapped compounds can be used for visualisation or quality assessment of the GSMN; and conversly, unidentified metabolites highlight gaps in the network and create model curation opportunities. This is especially important for specialised metabolism that is currently largely overlooked in GSMNs. Such mapping is thus attractive but it remains cumbersome due to several challenges such as harmonisation and matching of identifiers between metabolomic annotation profiles and GSMNs, and dispersion of information across various knowledge bases and input files. Currently, mapping requires manual or semi-manual mapping, but it is quite fastidious and prone to errors.

To overcome these challenges, we developed MetaNetMap, a Python package that automatically matches metabolite information between metabolomic annotations and GSMNs. It improves mapping rates through direct mapping taking into account metadata of input files, indirect matching by relying on conversion data tables built from third-party knowledge bases, and partial matching techniques. It offers an automatic solution for ambiguous mapping, providing relevant information for manual curation.

By automating and harmonising metabolite mapping, MetaNetMap aims to overcome a major barrier in multi-omic integration, enabling more efficient and reproducible integration of metabolomic data onto GSMNs.

Oral 17 – O 17

NMRSCOUT: a dereplication tool integrating multi-dimensional NMR with machine learning

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Dereplication of specialized metabolites in NMR spectra of complex mixtures remains a major challenge in natural product chemistry. Combining ^{1}H with ^{13}C, which presents a larger spectral width, and 2D methods (COSY, HSQC), which disperse signals in two dimensions, reduces the severe spectral overlaps of 1D ^{1}H NMR compromising signal annotation. However, annotation remains complex due to limited spectral databases for natural products.

To overcome these limitations, we developed NMRSCOUT, a dereplication tool integrating ^{1}H, ^{13}C, COSY and HSQC with machine learning. For a user-defined candidate list, NMRSCOUT predicts ^{1}H and ^{13}C chemical shifts using a Scalable Graph Neural Network with Morgan fingerprints, then reconstructs 2D spectra automatically. Predicted and experimental spectra are then compared using STOCSY and RANSY statistical filtering.

Validated on the BMRB, maximum mean absolute errors between predicted and experimental shifts reach 0.236 ppm (^{1}H) and 1.732 ppm (^{13}C) in CDCl, and 0.112 ppm (^{1}H) and 1.398 ppm (^{13}C) in DO. NMRSCOUT was then applied to 3,250 candidate metabolites of the genus Aspergillus from NPAtlas and the Dictionary of Natural Products (DNP), and predicted signals were searched in the ^{1}H, ^{13}C INEPT, ultrafast COSY and HSQC SYMAPS spectra acquired on Aspergillus chevalieri extracts. Using ^{1}H alone without statistical filtering, 99.7% of candidates obtained high scores, reflecting spurious matches. Combining the four experiments with STOCSY and RANSY statistical filtering, approximately 180 candidates presented high scores (90–100), the majority of which were confirmed by mass spectrometry, demonstrating effective candidate discrimination through NMR complementarity and statistical filtering.

Oral 18 – O 18

Mass spectrometry imaging for biofilm metabolomics study

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Bacterial biofilms, structured microbial communities encased in an extracellular matrix, exhibit strong resistance to both antibiotics and immune defenses, posing a significant challenge in treating persistent infections. Pseudomonas aeruginosa, an opportunistic pathogen, is particularly relevant in cystic fibrosis lung infections. To unravel the mechanisms behind biofilm persistence, innovative approaches are essential. Mass spectrometry imaging (MSI) emerges as a powerful tool, enabling the detection, localization, and characterization of metabolites within biofilms.
This project focused on developing and optimizing P. aeruginosa biofilm models for MSI analysis. Two models were established: an in vitro model using polydimethylsiloxane to simulate biomedical device colonization, and an ex vivo model using lung explants to study bacteria-host interactions. Various embedding materials were tested to preserve biofilm integrity during sectioning, with particular attention paid to compatibility with MSI. MSI was carried out with an AP-MALDI ionization source coupled to a hybrid quadrupole-orbitrap mass analyzer to map biomolecule distribution within these models.

The results highlighted MSI's ability to reveal biofilm heterogeneity, detecting metabolites involved in biofilm regulation and communication. Notably, key quorum sensing metabolites are annotated thanks to high mass measure precision and MS/MS spectra. In particular, PQS and HHQ exhibited distinct spatial distributions, with PQS concentrated in dense biofilm layers and HHQ dispersed throughout. Phenazine derivatives, like pyocyanin, showed increased production in lung explant biofilms, suggesting tissue invasion.
This work underscores the potential of MSI combined with advanced biofilm models to explore molecular profiles, offering insights into biofilm persistence and potential biomarkers to develop novel anti-biofilm strategies.

Oral 19 – O 19

Comprehensive SPE-LC-HRMS mapping of phase II steroid metabolites to reveal endometriosis complexity

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Endometriosis is a steroid-dependent disorder affecting approximately 10% of women of reproductive age worldwide. Despite extensive research, its etiology and physiopathology remain poorly understood, and reliable clinical non-invasive clinical biomarkers are still lacking. Because endometriosis is strongly modulated by estrogenic activity, phase II steroid metabolites, particularly sulfate and glucuronide conjugates, have emerged as promising molecular candidates for understanding disease mechanisms. Analytically, phase II steroid metabolism produces highly informative MS signatures, such as specific fragment ions and characteristic neutral losses, which greatly facilitate confident identification in complex biological matrices.

Here, we developed a sensitive, robust and scalable LC-HRMS method relying on online solid-phase extraction (SPE) coupled to UHPLC and an Exploris 120 Orbitrap mass spectrometer. The workflow enables the semi-targeted acquisition of a broad range of conjugated compounds (including steroids and bile acids for endogenous compounds, as well as xenobiotic metabolites such as phthalates) through a strategy combining full-scan (FS), all-ion fragmentation (AIF) and data-dependent acquisition (DDA). The data processing pipeline integrates complementary tools: Compound Discoverer was used for feature annotation and structural hypothesis generation, while a custom R Shiny application was specifically designed for AIF-based deconvolution of conjugated species.

Using this analytical workflow, multiple conjugated compounds were confidently identified (confidence level 1 and 2) in serum samples from women with endometriosis. This approach will now be deployed in a case-control study stratified by endometriosis presence and stage (control, stage I-II and stage III-IV). The analysis will be extended to both serum and urine samples for shedding light on disease pathophysiology.

Oral 20 – O 20

Development of Orbitrap Isotope Ratio Mass Spectrometry analytical workflow for Natural Abundance Fluxomics

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Isotopic profiles of metabolites through Position Specific Isotope Analysis (PSIA) at natural abundance can reveal biochemical dynamics in cancer development. While classical ^{13}C-labelled fluxomic have expanded our understanding of metabolism, they remain limited by high costs, ethical constraints, and isotope dilution. These factors often hinder their use in large patient cohorts or long term clinical monitoring.
Small variations in isotopic composition, known as isotope fractionation, reflect disease-associated biochemical processes, including those linked to cell transformation1. PSIA captures intra-molecular isotopic information invisible to conventional omics, thus complementing to standard cancer surveillance methods (e.g., X-ray, Computed Tomography, MRI, endoscopies). In this study, we evaluated the potential of high-resolution Orbitrap Isotope Ratio Mass Spectrometer (Orbitrap IRMS) to characterize natural isotopologue profiles of glutathione (GSH) and glutamate, key metabolites in tumor reprogramming.

Full-scan and MS/MS acquisitions enabled the investigation of major and minor isotopologues (^{13}C, ^{15}N, ^{18}O, ^{2}H, ^{34}S), including multiply substituted species. High precision (SD< 0.5 ‰) was achieved on analytical standards with high sensitivity compatible with biological extracts. These preliminary results demonstrate that PSIA of GSH and glutamate from biological samples is feasible.

This workflow provides a novel framework for investigating metabolic dysregulation in Li-Fraumeni syndrome (LFS), a hereditary cancer predisposition caused by germline TP53. This approach offers promising perspectives for the early detection and identification of different cancer types in LFS patients, complementing traditional clinical surveillance.

Oral 21 – O 21

Microbiota - Host interactions during juvenile growth: exploration of interconnected metabolic networks

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The gut microbiota shapes animal growth across a variety of nutritional contexts. Although recent advances have been made, the molecular mechanisms that drive this mutualistic relationship remain largely unclear. One reason for this gap is the inherent complexity of the gut microbiota, which is predominantly bacterial and forms intricate nutritional and metabolic networks both among its members and with the host. Because of this complexity, no study to date has precisely quantified how-and to what extent-the microbiota's metabolic activities contribute to juvenile host growth.

The MicroMetabo project aims to map the metabolic networks of the gut microbiota and determine how they influence the availability and allocation of the host's metabolic resources during juvenile development, using Drosophila melanogaster larvae as the model host. To achieve this, we employ a straightforward gnotobiotic system that gives us complete control over diet, host genotype, and microbial composition, and we integrate large-scale metabolomics, targeted metabolite tracing, and genetic and biochemical approaches.

We applied nuclear magnetic resonance (NMR) spectroscopy together with mass spectrometry (MS) to investigate the metabolic behavior of two representative gut bacteria-*Acetobacter pomorum* and *Lactoplantibacillus plantarum*-which are naturally found in the fly gut. To explore metabolic interactions among the different players, the bacteria were cultured individually, in co-culture, and finally in the presence of Drosophila larvae. Both extracellular and intracellular metabolomes were examined and quantified using a combined NMR-MS workflow for metabolic profiling, complemented by 13C isotopic labeling to trace carbon fluxes.

Communications Flash

Oral Flash F 01 – Poster P 01

Study of the impact of storage conditions on the stability of metabolites in fecal samples for 1H NMR metabolomics analysis

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Introduction: Metabolomics is a well-established field whose clinical applications and potential for personalized medicine remain highly promising. Faecal metabolomics is a valuable approach for biomarker discovery, notably in hypertension and colorectal cancer. However, stool samples collected at patients' homes introduce significant logistical and pre-analytical challenges, especially regarding metabolite stability prior to laboratory processing.

Objective: This study aimed to evaluate the impact of storage conditions and processing delays on faecal metabolite stability.

Method: Stool samples from ten healthy volunteers were stored in two matrices (phosphate-buffered saline alone or supplemented with 0.02% sodium azide, an antimicrobial preservative). Samples stored at 4 ◦C were centrifuged after 0, 2, 4, 8, and 24 hours, whereas samples stored at room temperature were evaluated at 0 and 2 hours only. NMR spectroscopy enabled the identification and quantification of 28 metabolites. Statistical analyses were performed using paired t-tests and one-way repeated measures ANOVA to assess temporal and storage-related effects.

Results: No significant changes were observed between 0 and 2 h under either temperature condition. In PBS alone, three metabolites showed significant decreases over time: formate (from 2 h), and butyrate and methylamine (from 8 h). In PBS supplemented with sodium azide, five metabolites were significantly affected after 8 h: glutamate, lysine, and tyrosine increased, whereas formate and methylamine decreased. Overall, 22 of the 28 quantified metabolites remained stable across matrices and time points.

Conclusion: These findings underscore the impact of storage matrices on metabolite concentrations and support the development of standardized, clinically applicable protocols for faecal metabolomics.

Oral Flash F 02 – Poster P 02

Steroidome quantification by online SPE for LC-HRMS: towards a systematic application in endometriosis research

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Endometriosis is a systemic, steroid-dependent, inflammatory disease, affecting approximately 10 % of women of childbearing age. Despite the central role of steroids in the patho-physiology, little is known about the interplay between parent steroids and their metabolites (i.e. steroidome) in the mechanisms underlying the disease. Due to their relatively low endogenous concentrations in blood and their chemical structure similarities, steroid quantification in biological fluids using LC-MS remains difficult and requires long and expensive sample preparation methods to reach physiological levels. In our project, Vanquish Duo system has been adapted for include online solid-phase extraction (SPE) configuration. The system is coupled to HRMS for the simultaneous quantification of 43 steroids.

Three analytical strategies were developed to enable the measurement of these steroids from 5 classes of compounds : corticosteroids, progestagens, androgens, estrogens and sulfo-conjugates. The workflow combines online SPE rapid and effective purification of sample with chromatography. This final configuration enhances reproducibility and selectivity, maintains high sensitivity, and allows short overall analysis times. The method operates in full scan acquisition mode using dual ionizations sources (ESI negative, APCI positive). The first results obtained from patient serum provide an overview of the blood steroidome and demonstrate the analytical performance of the method.

This approach establishes a reliable technical foundation for research and clinical applications that require fast, automated and integrated sample preparation scalable to large cohorts. The method is versatile and may be adapted to other matrix of interest for endometriosis and in the short-term, applied in a real case-control study.

Oral Flash F 03 – Poster P 03

Surrogate Internal Calibration Strategies for Extended Absolute Quantification by LC-MS/MS

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Absolute quantification is essential in metabolomics for characterizing metabolite concentrations as indicators of physiological states or diseases. Multi-targeted internal calibration (IC) using stable isotope-labelled standards (SILs) has emerged as an attractive approach for endogenous analyte quantification, avoiding the need for blank matrix preparation. However, commercial SIL availability is limited, costs are high, and purity can be restricted. Heterologous internal calibration (HIC), employing alternative SILs as surrogate calibrants for multiple analytes, addresses these limitations through response factor determination between target metabolites and selected SILs.

HIC was first applied to plasma samples from a chronic kidney disease cohort, quantifying 18 endogenous metabolites by LC-MS/MS, primarily from the tryptophan pathway. A reduced panel of five heterologous SILs effectively quantified all 18 analytes, achieving trueness within 70–130% and precision below 10% for most compounds, with performance comparable to matched homologous SILs.

This methodology was then extended to a broader steroid panel by incorporating post-column infusion (PCI) correction for sample-specific matrix effects. In this approach, response factors are determined in neat solvent while matrix effects are corrected individually per sample. Each data point of the analyte peak is normalized by the corresponding continuously infused standard signal, enabling reconstruction of a corrected chromatographic peak for accurate quantification.

For steroid analysis, exogenous internal calibrants, structurally similar non-endogenous compounds, were investigated as surrogate standards to overcome limited SIL availability. Combined with PCI correction, this strategy maintained quantitative performance while providing a practical, scalable, and cost-effective solution for large-scale metabolomics studies.

Oral Flash F 04 – Poster P 04

Integration of 1D and fast 2D (UF-COSY, NUS-HSQC, NUS-TOCSY) NMR metabolomic and lipidomic datasets applied to mice liver samples

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A national project was conducted within the MetaboHub infrastructure to investigate the complementarity and redundancy of metabolomics and lipidomics analytical methods, applied on the p53 tumor suppressor and several of its key regulators. The project involved untargeted NMR approaches, especially fast 2D NMR spectra for enhanced signal separation and integration compared to 1H NMR. The assessment of their statistical performances and their advantages in terms of annotation is explored.

Lyophilized livers of 112 mice (fed or fasted) harvested from liver-specific conditional knock-out mice for p53, Mdm2 and E4f1 (eight genotypes) were extracted using the Bligh and Dyer protocol. 1H and NUS-TOCSY experiments were conducted on the metabolomic extracts while 1H and fast 2D (UF-COSY, NUS-TOCSY, NUS-HSQC) were performed on the lipid extracts. 1D spectra were processed using TopSpin and NMRProcFlow, while various software were tested for 2D datasets, including DeepPicker, PeakViewer and APPIN. Exhaustive annotation was performed by leveraging the complementarity between the 1D and 2D datasets. Then, statistical analyses were conducted using non-supervised (ComDim) and supervised (ConsensusOPLS) multiblock approaches.

Multiblock analyses revealed better statistical performances by integrating the six datasets together. These analyses distinguished fed from fasted groups, but not genotypes. Lipidomic datasets contributed more than metabolomics ones to this separation, showing that lipids are more impacted by the mice's diet than polar metabolites. For lipidomics, NUS-TOCSY and UF COSY demonstrated similar contributions to the model as the 1D dataset, while the use of all 2D datasets allowed the annotation of 53 lipid signals with increased confidence.

Oral Flash F 05 – Poster P 05

Du champ à l'assiette: transfert des effets du génotype et des procédés de transformation du colza sur la santé animale et humaine dans une approche One Health

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Le colza est la principale plante oléo-protéagineuse cultivée en France. Riche en composés bioactifs antioxydants et anti-inflammatoires, il constitue un levier potentiel pour améliorer la santé animale et humaine. Dans ce projet, nous étudions le transfert de l'effet combiné du génotype et des procédés de fabrication des tourteaux du champ à l'assiette, dans une approche intégrée One Health.

Deux génotypes contrastés, Mambo et Bonanza précédemment sélectionnés pour leur propriété antioxydante (+ et -, respectivement), ont été transformés selon deux procédés : une méthode conventionnelle dégradante et une méthode optimisée préservant les bioactifs. Des vaches gestantes ont été nourries pendant neuf semaines avec quatre régimes expérimentaux. Le lait produit a ensuite alimenté leurs veaux et des souris ob/ob pris comme proxy humain et constituant deux modèles animaux du stress oxydatif. Le métabolome primaire a été analysé dans le plasma des vaches, dans leur lait, ainsi que dans le plasma des animaux consommateurs de ce lait (veaux et souris), par métabolomique suspect screening et des analyses statistiques multivariées.

Le régime Mambo optimisé induit une signature métabolique distincte, associée aux voies du stress oxydatif, de l'inflammation et du métabolisme musculaire. Ces différences se retrouvent dans le lait et chez les animaux consommateurs. Les marqueurs du stress oxydatif (isoprostanöıdes) et de l'inflammation (PGE2, PGF2), dosés par LC-HRMS, diminuent significativement avec ce régime. Ces résultats montrent que le génotype et le procédé technologique influencent la qualité des tourteaux, la santé des vaches et des consommateurs de leur lait, illustrant pleinement le concept One Health.

Oral Flash F 06 – Poster P 06

Uncovering the diversity and ecological roles of glucosinolates in rapeseed seed exudates

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To promote sustainable food production and reduce reliance on synthetic pesticides, biobased alternatives are being developed to enhance crop resilience while preserving environmental quality. In this context, we investigated rapeseed seeds and their spermosphere (the zone surrounding germinating seeds) to identify natural compounds involved in defence against biotic stress. The spermosphere of ten rapeseed genotypes grown under two contrasting crop management systems was characterized using LC-MS2 untargeted metabolomics. We elucidated the molecular and metabolic mechanisms underlying seed exudation by integrating metabolomic and multi-omic approaches, considering plant metabolites and interaction with associated microorganisms, and viewing seed as an holobiont, a functional ecological unit composed of the plant and its microbiota.

Glucosinolates were rapidly exuded and were abundant in the spermosphere, with strong genotypic variation. Although their role in plant–herbivore interactions is well established, their ecological function in seeds and exudates remains poorly understood. Identified GSLs and their degradation products were mapped onto biosynthetic pathways and quantified in both seeds and exudates from genotypes with contrasting glucosinolates contents.

Exudates, together with more than ten glucosinolates and related degradation products were evaluated for antimicrobial activity, several showing strong inhibitory effects. Since glucosinolates were mainly localized in the embryo prior to exudation, multi-omic analyses were conducted to investigate genes and enzymes involved in their biosynthesis, transport, degradation, and modification during seed exudation, across different seed tissues and in the exudates. Overall, our results reveal metabolic diversity in the spermosphere and demonstrate a key ecological role for glucosinolates in seed–pathogen interactions during germination.

Oral Flash F 07 – Poster P 07

Seeds as ecosystem engineers: metabolomic programming of spermosphere microbial assembly and early-life resilience in common bean

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Germinating seeds actively shape their surrounding microenvironment, the spermosphere, through the release of a complex mixture of primary and specialized metabolites that modulate microbial assembly, creating conditions that support successful establishment of the autotrophic seedling. In common bean (*Phaseolus vulgaris*), we characterized the spermo-sphere of eight genotypes grown in two contrasting environments. We demonstrated that both genotype and production environment determined the composition of seed exudates and associated microbial communities, revealing genotype-specific chemical signatures correlated with distinct microbial assemblages. Additionally, the activity of selected metabolites on microbial growth was experimentally validated, confirming their functional role in shaping these communities. Building on these insights, we investigated how seed physiological status, particularly aging and vigour loss, alters spermosphere chemistry and microbial interactions. Using integrative multi-omics approaches, including untargeted metabolomics and microbiome profiling, we characterized how genotype, environment, and seed aging collectively influence metabolite–microbe associations, including interactions with potential beneficial or opportunistic microorganisms. This framework positions the seed as an ecosystem engineer, orchestrating its microbial niche through biochemical signalling, with early-life implications for resilience, establishment success, and buffering against environmental and biotic stress. These studies provide the first comprehensive view of how genetic, environmental, and physiological factors converge to shape spermosphere dynamics and highlight the functional significance of seed exudates in plant–microbe interactions. By linking metabolomic signatures to microbial assembly and potential seed vigour outcomes, this work offers a novel conceptual and methodological foundation for understanding early plant establishment and informs strategies for sustainable crop production, aligning with One Health principles.

Oral Flash F 08 – Poster P 08

Comparison study of monocotyledonous and dicotyledonous seeds for their stilbenoid content

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Phenolic compounds are specialized plant metabolites that encompass several classes, including phenolic acids, flavonoids, tannins, and stilbenoids such as resveratrol and ϵ-viniferin. Stilbenoids have attracted considerable attention due to their significant roles in plant physiology and their potential benefits for human health. These compounds are synthesized either constitutively or are induced in response to environmental stresses. They have been identified in different plant organs, including roots, leaves, bulbs, flowers, and seeds. To date, approximately 200 species of Monocotyledons and Dicotyledons have been reported as producing stilbenoids. However, given that Angiosperms comprise nearly 250,000 species, a substantial proportion of plant diversity remains unexplored. In this study, we selected more than 400 species that we obtained from botanical gardens to assess their stilbenoid content. The analysis focused specifically on seeds, organs for which data remain scarce. Following grinding, phenolic compounds were extracted and analyzed using a non-targeted metabolomics approach based on UHPLC-HRMSn. Particular emphasis was placed on the characterization of stilbenoid profiles. We noted some plant families, such as Iridaceae, with a particular richness in these compounds.

Oral Flash F 09 – Poster P 09

Deciphering the vanadium dependent haloperoxidase roles under oxidative stress in a brown alga using knock-out mutants, transcriptomic and metabolomic analyses

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Some brown algae are known to concentrate halogens as bromine or iodine. They are also producing halogenated metabolites likely involved in signaling and/or in defense during biotic interactions and physiological responses to environmental changes. These particular metabolites and their biosynthesis are still poorly described. Furthermore, the processes and function of halogenation remain uncertain in these marine organisms. To address this gap, we explored the production of these metabolites and their role in brown algae using omics approaches. A key gene putatively involved in halogenation, the vanadium-dependent Bromoperoxidase (vBPO), was inactivated via CRISPR-Cas9 method in the model brown alga *Ectocarpus sp7*. We compared KO and wild-type strains combining physiological observations, gene-regulation analysis by RNA sequencing, chemical and metabolomic profiling by ICP-MS and UHRLC-MS/MS.

Although the different strains appeared to grow similarly, metabolomic analyses showed distinct patterns, particularly in polar and reserve lipids between the WT and mutant strains. Also, the photosynthetic efficiency of the KO strains was reduced at high light intensities. When the strains were exposed to oxidative stress for 24 hours, preliminary transcriptomic and metabolomic analyses revealed stress response patterns. Differences between WT and KO strains were still present, but the same temporal trend was observed. Finally, in order to identify different halogenated compounds depending on the strain, we will investigate the metabolome of stressed and non-stressed algae using a SBSE approach.

Overall, this work will provide new knowledge about the chemical diversity, particularly on specific metabolites regulated through vBPO and their biosynthesis pathways in a brown algae model.

Oral Flash F 10 – Poster P 10

Investigating conserved metabolites and associated biosynthetic pathway in seeds: The CoreSeedMet Project

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Plant metabolomics has largely focused on characterizing the diversity and, to a lesser extent, the function of specialized metabolites (SMs), predominantly in vegetative tissues. In contrast, the existence of a conserved set of SMs shared across diverse taxa remains largely unexplored, especially in seeds. Such shared distribution could reflect either ancient evolutionary conservation or convergent adaptation. Characterizing conserved seed metabolites may also help refine the conceptual definition of specialized metabolites.

This project tests the hypothesis that a subset of seed specialized metabolites, particularly flavonol derivatives, is evolutionarily conserved across plant lineages because these compounds enhance seed survival and reproductive success. Quercetin and kaempferol derivatives are considered primary candidates for the core seed metabolome, as they have been consistently detected in our multi-species LC-MS2 dataset over five years, including Brassicaceae, Poaceae, and additional families. Flavonols, especially quercetin-based structures, contribute to antioxidant defence, pathogen resistance, and seed protection.

Over the past five years, our team has compiled LC-MS2 data on seed SMs from a wide range of species. We recently expanded this dataset to include cultivated species from previously underrepresented families; it now encompasses more than 60 plant species and approximately 1,000 genotypes, representing broad metabolomic diversity.

We aim to identify a conserved core seed metabolome and its biosynthetic networks using a comparative multi-species, multi-omics framework integrating metabolomic, genomic, and protein structural data to investigate the enzymatic basis of flavonol accumulation and conservation, and assess whether pathway conservation is associated with conserved biological functions relevant to crop resilience and seed performance.

Oral Flash F 11 – Poster P 11

Révéler l'inconnu : Anchor Based Molecular Networking, un outil pour l'identification des Nouveaux Produits de Synthèse

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Les Nouveaux Produits de Synthèse (NPS) sont des substances psychoactives conçues pour imiter les effets de drogues contrôlées tout en échappant aux réglementations. Leur émergence rapide et leur diversité structurale rendent leur identification difficile, nécessitant des approches analytiques non ciblées basées sur la chromatographie liquide couplée à la spectrométrie de masse haute résolution (LC-HRMS) pour leur détection dans des matrices biologiques. Cependant, ces stratégies génèrent de grands volumes de données MS/MS, dont l'interprétation reste complexe et chronophage.

Le réseau moléculaire (RM) permet d'organiser ces données selon leur similarité spectrale, mais son exploitation dépend de la présence de nœuds d'intérêt identifiés. Dans cette perspective, une stratégie de réseau moléculaire ancré (ABMN) a permis de faciliter l'annotation des NPS dans des échantillons biologiques. Des composés de référence ont été introduits au sein du RM, comme repères pour guider la propagation de l'annotation de composés inconnus apparentés. Un panel de standards couvrant les principales classes de drogues et NPS a été analysé conjointement à des échantillons biologiques de patients intoxiqués, par LC-HRMS.

L'approche ABMN a permis, sans information préalable, l'identification de plusieurs NPS et de leurs métabolites. L'exploration autour des nœuds d'ancrage a permis l'identification de composés structurellement apparentés, tels que le bromazolam par regroupement avec des benzodiazépines synthétiques ou la N-éthylnorpentédrone et ses métabolites N-désalkylés, réduits et hydroxylés, renforçant la fiabilité de l'annotation.

L'outil ABMN constitue une stratégie prometteuse pour l'identification de composés inconnus et de leurs métabolites dans des matrices biologiques, transposable pour des études exposomiques.

Oral Flash F 12 – Poster P 12

Integrated multi-block fast multi-dimensional NMR metabolomics and lipidomics

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In metabolomics, ^{1}H NMR experiment is widely used thanks to its short acquisition time and the possibility to achieve a global quantitative profiling with simple sample preparation. In complex mixtures, however, most of the signals are overlapped, and the signal integration step, or bucketing, results in variables shared by multiple metabolite signals, affecting the data analysis performance. By using 2D NMR, signals spread along a second dimension, increasing their separation and thus minimizing shared buckets, while Ultra-Fast (UF) and Non-Uniform Sampling (NUS) strategies make their acquisition duration usable in a metabolomics context. This study aims to take advantage of the systematic acquisition of fast 2D NMR experiments on samples to increase the discriminative power of NMR-metabolomics approaches. To this end, ^{1}H NMR and fast 2D (UF COSY, NUS zTOCSY and NUS HSQC) NMR spectra were acquired on serum samples from pigs exposed or not to Bisphenol-A (BPA), following extraction using a Bligh and Dyer protocol. Both lipidic and metabolic extracts were analyzed, resulting in eight integrated data matrices. After PQN normalization, autoscaling and variable selection by MC-UVE, multiblock modeling using Consensus OPLS-DA successfully separated both groups in contrast to ^{1}H NMR metabolomics alone. For metabolomics, fast 2D NMR blocks contributed more strongly to the separation, whereas in lipidomics, ^{1}H NMR contributed the most due to reduced overlapping, demonstrating the complementarity of these experiments. Annotation of high-VIP-score variables confirmed the metabolic disruptor character of BPA with perturbations previously reported in the literature, supporting the robustness and transposability of our approach.

Oral Flash F 13 – Poster P 13

Deciphering mechanisms of service plants involved in the disruption of host plant recognition by a specialist insect herbivore thanks to complementary volatolomic approaches

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Plant volatolome is a very diverse chemical universe which is deeply explored for fragrance and organoleptic applications but also for chemical ecology purposes because of its proven role as mediator in biotic interactions. Especially, olfaction plays a fundamental role in key insect behaviors, such as the search for a suitable host plant. However, these mechanisms are complex and require exhaustive qualitative and quantitative characterization of the volatolome.

Crop diversification strategies, including the use of service plants, offer promising tools to manipulate pest behavior by disrupting host recognition. For instance, field experiments have demonstrated that *Calendula officinalis* can disrupt the oviposition behavior of *Delia radicum*, a major specialist pest of brassica crops during early growth stages. This study aimed to unravel the volatile compounds involved in this disruption.

Volatile Organic Compounds (VOCs) from the service plant, *C. officinalis* and a host plant, *Brassica oleracea* were both trapped in Dynamic Headspace and extracted under vacuum using Vacuum Assisted Sorbent Extraction (VASE) followed by thermal desorption coupled with GC-MS. These two approaches allowed us to explore the largest possible diversity of VOCs in order to analyze the impact of the interaction between the two species on the characteristics of their volatolome. Indeed, VASE, due to its high extraction capacity, facilitated identification and quantification of discriminatory compounds in co-cultivated plants, whereas Dynamic Headspace better reflected realistically emitted VOCs.

Further GC-EAD analyses revealed specific compounds from the service plant volatolome perceived by the fly, suggesting their involvement in host plant recognition disruption.

Communications Posters

Poster P 14

Approche isotopique en métabolomique et fluxomique pour l'identification de biomarqueurs du cancer du sein par GC-C-IRMS

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Le développement de biomarqueurs fiables pour le diagnostic précoce, le pronostic et le suivi thérapeutique du cancer du sein constitue un enjeu majeur en métabolomique et en fluxomique. Dans ce contexte, l'analyse des signatures isotopiques représente une approche innovante pour explorer les altérations métaboliques, notamment au niveau du métabolisme lipidique tumoral.
Une méthode précédemment développé basée sur la chromatographie en phase gazeuse couplée à la spectrométrie de masse de rapports isotopiques (GC-C-IRMS) a permis l'analyse quantitative et isotopique d'acides gras libres dans des matrices biologiques complexes. Cette approche repose sur une préparation simplifiée incluant une saponification sans dérivation, limitant ainsi l'introduction de carbone exogène et des biais isotopiques associés.

La méthode a été appliquée à une cohorte de 150 patientes atteintes de cancer du sein, incluant tissus tumoraux, tissus adjacents et sérums (n = 450 échantillons). Les principaux acides gras (C14:0, C16:0, C18:0, C16:1, C18:1, C18:2) ont été quantifiés et caractérisés isotopiquement. La validation a démontré d'excellentes performances analytiques.

Les résultats révèlent des variations significatives de $\delta^{13}C$ entre tissus cancéreux et non cancéreux, suggérant une reprogrammation métabolique associée à une augmentation de la lipogenèse de novo. Les signatures isotopiques sériques indiquent un potentiel en tant que biomarqueurs non invasifs permettant également la discrimination de sous-types tumoraux. Cette approche ouvre de nouvelles perspectives en fluxomique isotopique en abondance naturelle pour l'étude du métabolisme tumoral et le développement de biomarqueurs en oncologie.

Poster P 15

Benchmarking deep learning models for cardiac aging estimation and building heart-specific metabolomic clocks

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Biological aging reflects the progressive decline of biological systems across multiple molecular and functional scales. Among emerging biomarkers, ECG-based deep learning models can estimate heart-specific chronological age and capture functional cardiac aging. However, the generalizability of pretrained models across independent cohorts remains unevaluated, limiting their adoption in population-based settings.
We evaluated pretrained deep learning architectures for ECG analysis, including convolutional neural networks and transformer-based foundation models trained using self-supervised learning, benchmarked on PTB-XL (n=21,373). Self-supervised representations substantially outperformed supervised diagnostic features, with the best architecture achieving MAE=8.2 years and R2=0.59, compared to MAE=13.0 years and R2=–0.10 for the supervised baseline, demonstrating that general-purpose ECG representations transfer more effectively to age prediction than task-specific embeddings.

To complement ECG-derived estimates, we developed a metabolomic aging clock in the MetaCardis cohort (n=2,105) using plasma metabolomics (1,514 metabolites) and ElasticNet regression with 5-fold cross-validation. The clock explained 63.6% of variance in chronological age (MAE=5.54 years), retaining 476 predictive metabolites, confirming that circulating metabolites track age-related biological signals across cardiometabolic disease groups.

We implemented a standardized preprocessing and evaluation pipeline with consistent metrics (MAE, R2) across both modalities. Pretrained ECG models will subsequently be applied to the Canadian Longitudinal Study on Aging (CLSA; n=51,000), enabling assessment of generalizability with matching metabolomics data.
This work establishes a methodological foundation for an interpretable cardiac aging clock and its integration with metabolomic clocks within a unified biological aging framework, aimed at identifying individuals with accelerated aging and improving cardiometabolic disease trajectory prediction.

Poster P 16

Nitrogen Isotope Signatures of Amino Acids: A Promising Tool for Lung Cancer Tissue Characterization

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Lung cancer remains a leading cause of cancer-related mortality, often characterized by late diagnosis and complex metabolic heterogeneity. While traditional histology is essential, there is a critical need for new molecular biomarkers to better characterize tumor metabolism and improve diagnostic precision.
To advance biomarker discovery in oncology, we applied natural abundance stable isotope analysis to investigate tumor-associated alterations in nitrogen metabolism. Using gas chromatography–combustion–isotope ratio mass spectrometry (GC-C-IRMS), we measured $\delta^{1}N$ values of amino acids in paired clinical specimen, comparing lung cancer tissue with adjacent non-tumoral tissue from the same patients.

A derivatization protocol for methyl ester pentafluoropropionic derivatives was implemented to achieve compound-specific $\delta^{1}N$ measurements across 16 amino acids. The method demonstrated high analytical performance in terms of linearity, precision and stability, proving its suitability for complex clinical biopsy matrices.
Our results revealed distinct $\delta^{1}N$ patterns between tumor and adjacent tissues, reflecting a significant cancer-associated reprogramming of nitrogen metabolism. These findings highlight the potential of compound-specific nitrogen isotope profiling as a powerful tool for metabolic characterization and a promising avenue for biomarker development in lung cancer diagnosis.

Poster P 17

Couplage chromatographie / ExcedIon Pro pour le profilage et la quantification de stéroïdes dans des tumeurs de la glande surrénale

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Le cortex surrénal produit des stéroïdes via une cascade enzymatique, principalement des réactions d'oxydation par des CYP450, dont le cholestérol est le précurseur. Les stéroïdes sont impliqués dans de nombreux processus physiologiques et leur métabolisme est altéré dans les tumeurs corticosurrénales. Bien que la stéroïdogenèse soit en partie caractérisée, les fortes similarités structurales entre les stéroïdes (nombreux stéréoisomères différenciés par la position des oxydations sur le squelette) et leurs difficultés d'ionisation son l'exploration. Ce travail vise à développer et optimiser des méthodes sur Orbitrap ExcedIon Pro en LC et SFC-MS/MS, afin d'explorer la stéroïdogenèse et d'évaluer l'impact des cancers de la surrénale sur celle-ci. Les méthodes analytiques ont été optimisées à l'aide de dix standards stéroïdiens, permettant de suivre la séparation de trois isomères (21-désoxycortisol, corticostérone et 11-désoxycortisol). Comparativement avec d'autres méthodes déjà développés au sein du laboratoire sur TimsTOF, un facteur 10 en gain de sensibilité en full scan a été observé. L'emploi du tSIM2 a encore un gain de sensibilité, générant des limitent de détection proche de celles obtenues en ciblée sur TSQ-ALTIS, l'appareil utilisé en routine à l'hôpital pour doser les concentrations des stéroïdes dans les échantillons de patients. Les méthodes en full scan et eDR ont ensuite été appliquées à l'analyse d'extraits stéroïdiens issus d'échantillons de tissu surrénal provenant de sujets témoins et de patients atteints d'un carcinome cortico-surrénalien. Les dix stéroïdes couramment mesurés en routine ont été détectés, ainsi que 10 autres composés peu courants nécessitant une confirmation par analyse de fragmentation.

Poster P 18

Effets des cyclodextrines sur la synthèse des polyphénols dans des cultures in vitro de *Vitis vinifera* cv Gamay Teinturier

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Les suspensions cellulaires de *Vitis sp.* sont un matériel adapté pour la production de métabolites d'intérêt tels que les polyphénols. L'utilisation des cyclodextrines (CD), est un bon outil pour stimuler la production de ces composés.
Jusqu'alors, les études ne se sont intéressées qu'à un unique type de CD, (la β) et sur des molécules majoritaires. Nous avons mené une étude métabolomique ciblée sur les polyphénols par HPLC-HRMS pour mieux détailler les effets de trois types de CDs (α, β et γ) à trois doses et à 3 jours.

Concernant l'analyse intracellulaire, 34 polyphénols ont été quantifiés. La β-cyclodextrine influence la production des flavanols et notamment de la procianidine B4 mais aussi de certains stilbènes monomériques comme le resvératrol. Toutefois, la concentration en dimères de stilbènes, comme la δ-viniferine diminue et tend à disparaître totalement. Pour ce qui est de la γ-cyclodextrine, elle suit cette tendance avec toutefois des effets plus modérés concernant la synthèse des flavanols. Enfin, l'ajout d'α-cyclodextrine ne confère que peu de variations par rapport aux cellules témoin.

Par ailleurs, au sein du milieu extracellulaire, on remarque une présence élevée en resvératrol relative à l'ajout des CDs. Nonobstant cet effet n'est pas observé pour les flavanols. Cela met en lumière une différence entre l'intra et l'extra cellulaire.
Suite à l'effet des différentes CDs, il pourrait être intéressant d'étudier l'effet cumulé de ces éliciteurs avec d'autres agents tels que le méthyljasmonate.

Poster P 19

Exploring the specialized metabolite diversity and biosynthesis of *Marchantia polymorpha* oil bodies

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Plants produce a vast array of specialized metabolites (SMs) that play crucial roles in their interactions with the environment. Furthermore, these molecules display a wide range of activities, making them valued in several industrial sectors.

Aromatic and exotic plants have been widely used for identifying pharmacologically interesting compounds. Inversely, the metabolic richness of bryophytes (non-vascular plants including mosses, liverworts and hornworts) has been neglected until recently. Interestingly, liverworts, including Marchantia polymorpha, produce various characteristic terpenoids (usually sesquiterpenes) and some flavonoid-related benzenoid compounds named bisbibenzyls that display a broad spectrum of biological activities, including toxicity to bacteria, fungi and viruses. Moreover, a wide range of those SMs are accumulated in liverwort specific organelles named oil bodies (OBs). While the existence of these organelles is known for decades, their precise metabolite composition, biosynthesis and function remain largely unknown.

Multi-omic analyses (untargeted metabolomics (LC-MS/MS) and proteomic analyses (LC-MS/MS)) are currently ongoing on control and wounded thalli samples from M. polymorpha mutants lacking or over-expressing OBs (Mperf13ge and Mperf13GOF) and wild-type genotype (Tak-1). Those results will provide a comprehensive overview of the OB specialized metabolic network. Furthermore, a protocol to isolate and purify M. polymorpha OBs is being settled with the aim of further precising those results by performing the omic analyses on purified OBs.
Besides providing insights into the metabolic machinery underlying OBs specialized metabolism, the results obtained would set a basis to establish Marchantia as a promising model for synthetic metabolic biology and a source of pharmacologically interesting molecules.

Poster P 20

Dynamics of specialized metabolite homeostasis and regulation in plants and seeds to improve iron nutrition

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Iron (Fe) is an essential element for the nutritional quality of plants and seeds. Its low bioavailability in alkaline soils limits both its acquisition and its accumulation in harvestable organs. In non-grass plants, coumarin specialized metabolites play a key role in iron mobilization by chelating Fe(III) and facilitating its uptake at the root level. However, the molecular mechanisms governing the transport and compartmentalization of Fe–coumarin complexes, as well as their impact on iron accumulation in seeds, remain poorly understood. The DYNAFER project aims to identify and characterize the genes involved in these processes in Arabidopsis thaliana. Here we show that a combined screen integrating coumarin-based phenotyping and seed ionomics in an ethyl methanesulfonate (EMS) mutant population enables the identification of genetic determinants of seed iron accumulation. A population of more than 600 homozygous lines was used and phenotypically screened based on their response to coumarin in order to identify lines with altered coumarin dynamics. In parallel, seeds from EMS lines were analyzed by ICP-MS to quantify macroand micro-elements. Ten candidate lines displaying significantly altered responses to fraxetin or to iron contents compared to the wild-type Col-0 were retained. If successful, this work will establish a functional link between root coumarin dynamics and plant and seed iron accumulation, further elucidating the systemic role of these, and possibly other specialized metabolites, in plant and seed mineral nutrition. These findings support crop biofortification, especially in regions where soil alkalinization threatens global food security in the context of climate change.

Poster P 21

SCPL17 enzyme mediates glucosinolate acylation in Arabidopsis seeds under heat stress

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Plants produce thousands of specialized metabolites (SMs) with diverse biological activities critical in plant-environment interactions. Among these, glucosinolates (GSLs) massively accumulate in seeds of Brassicaceae, including the model species Arabidopsis thaliana, where GSLs are synthetized in the funiculus, transported to the seeds, and subjected to structural modifications. While some GSL negatively impact seed quality and can be toxic, others have antioxidant and health benefits. In addition, GSLs are essential for seed resistance to stress. GSLs present a core structure: a sulfated isothiocyanate group conjugated to a β-thioglucose and a side-chain that can be aromatic, indolic, or aliphatic. The structural diversity of GSLs arises from different functional groups added to the core structures, including acylation (i.e. sinapoylation and benzoylation). In this work, we show that A. thaliana seeds subjected to high temperatures (HT) accumulate high levels of newly identified sinapoylated and benzoylated glucosinolates. Functional genomics and multi-omics analyses revealed that the production of these compounds is mediated by SCPL17, a serine carboxypeptidase-like acyltransferase. The scpl17 mutant exhibits reduced production of sinapoylated and benzoylated GSLs in seeds, particularly under heat stress. Furthermore, physiological analyses highlighted abnormal phenotypes in seeds of the spl17 knockout mutant subjected to HT. To characterize and confirm its enzymatic activity, SCPL17 recombinant proteins were expressed through heterologous expression in a yeast system. The resulting reaction products of the enzymes, glucosinolates and co-substrates, were analyzed by UHPLC-MS/MS.
Taken together these results suggest that SCPL17-mediated GSL acylation has an important role in A. thaliana seed responses and adaptation to HT.

Poster P 22

Gut–brain interactions in a Drosophila model of Parkinson's disease: NMR metabolomics approach

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The gut-brain axis is a major bidirectional communication system now recognized as being involved in the initiation and propagation of neuronal pathologies, including Parkinson's disease. Our NMR metabolomic study aims to provide a better understanding of brain-gut interactions in Parkinson's disease.
The fruit fly Drosophila melanogaster is a model of choice for the study of human disorders. This organism possesses homolog genes for about 70% of known human genes causing diseases. It is relatively cost and time effective, and the manipulation of gene expression in the fly is easily achieved.

Here we studied Parkinson's disease models developed in Drosophila, by the in vivo expression of a mutant pathogenic form of human α-synuclein (α-synA30P). In order to uncover reciprocal influences of these two organs during the development of the pathology, we expressed α-synA30P either in neurons and/or the gut in Drosophila.

We analyzed by NMR metabolomic modifications in the brain and gut, at early (10 day-old) and late (30 day-old) stages of the disease. Metabolites were extracted from the head and body of Drosophila. 1D 1H-NMR spectra were acquired on a 700 MHz spectrometer equipped with a cryoprobe. Statistical analyzes were performed to differentiate diseased Drosophila from their controls and detect reliable biomarkers.
Our results demonstrate interestingly that the two organs interact and influence each other at both stages of the disease. α-synA30P expression in the brain leads to rapid metabolic defects, visible in both organs, while the effects of its expression in the gut appear to be slower.

Poster P 23

Metabolism and Mechanisms of Hepatotoxicity of Nutmeg Phenylpropanoids Investigated by Untargeted Metabolomics and Chemometric Approaches

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Nutmeg is the seed of *Myristica fragrans*, a well-known spice commonly used in cookery. At high doses, nutmeg consumption can induce an adrenergic syndrome and psychogenic effects. These effects, mainly attributed to phenylpropanoid compounds such as Myristicin, may occur either intentionally in individuals seeking psychoactive experiences or accidentally following excessive consumption.
We investigated the metabolic pathways of nutmeg phenylpropanoids under in vitro conditions. Two hepatic cell lines were used: HepG2, characterized by low cytochrome P450 expression, and HepaRG, which exhibits a metabolically competent phenotype with higher cytochrome P450 activity. Cells were exposed or not to an ethanolic extract of nutmeg, and culture supernatants were collected at seven time points to evaluate metabolite kinetics. Supernatants were analyzed by UHPLC-HRMS/MS in data-dependent acquisition (DDA) mode, in both positive and negative electrospray ionization. Non-targeted metabolomics data were processed using a chemometric pipeline based on ANOVA-Simultaneous Component Analysis, justified by the longitudinal and multifactorial experimental design. Cell viability was also assessed using Alamar Blue and LDH assays.
Chemometric analyses enabled the identification of nutmeg phenylpropanoids and their metabolites, whose structures were further annotated by in silico dereplication. Comparison with non-exposed cells revealed nutmeg-induced variations in the endogenous metabolome, specific to each cell line and mainly involving amino acids. The kinetics of phenylpropanoid metabolism were characterized in a cell line-dependent manner. Finally, higher cell viability was observed in metabolically competent HepaRG cells, challenging previously proposed mechanisms of nutmeg hepatotoxicity attributed to phase I metabolites of myristicin.

Poster P 24

Decoding condensed tannins in faba bean (*Vicia faba* L.) seed coats: structural diversity across spring and winter varieties revealed by UHPLC-DAD-MS/MS and phloroglucinolysis.

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The faba bean seed coat represents a polyphenol-rich co-product of legume protein extraction with tannins levels varying widely among varieties. Residual tannins persist even after dehulling and may negatively affect protein techno-functional properties. Gaining deeper insights into tannin structure could help minimize these interactions or, alternatively, exploit them for innovative applications. Thus, we discriminated twelve varieties of faba bean (*Vicia faba* L.) for their seed coat composition and content in condensed tannins. Hydromethanolic extraction and phloroglucinolysis followed by liquid chromatography coupled to UV-Visible and mass spectrometry detection provided complementary data and enabled the in-depth characterization of the faba bean tannin fraction made of both procyanidin and prodelphinidin subunits. Spring types presented higher total flavan-3-ol content (81.7 ± 7.0 g.kg-1 DW), smaller tannins chains (mDP = 9.7 ± 0.8) and lower proportion of constitutive prodelphinidin subunits (59.4%) than winter types (flavan-3-ol = 70.8 ± 5.8 g.kg-1 DW, mDP = 10.6 ± 0.5, 64.8%).

Poster P 25

RICOCHETS: Resilience to recurrent heat stresses in plants

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The years 2015 to 2025 have shown the highest average temperatures ever recorded. Heat waves frequency also increased, impacting yield and quality of crops production. While plant responses to isolated heat stress are well documented, the plants responses to recurrent heat events-closer to natural conditions-still require further investigation. A deeper understanding of the plant mechanisms in heat stress response, during recovery phase, or by comparing isolated and recurrent heat waves, would provide valuable insights for identifying adaptive traits and developing more climate-resilient crop varieties.

The INRAE ANR RICOCHETS project focuses on sorghum to study plant responses to recurrent heat stress through controlled experiments that replicate realistic climate conditions. By using untargeted (LC-MS) and targeted metabolomics (i.e. analysis of biomasss composition) and studying biomass the project aims to evaluate whether consecutive heat stress events can have a cumulative effect on metabolism.

This integrated approach seeks to identify key metabolic pathways for breeding heat-resilient sorghum varieties. More than 50% of features significantly responded to heat waves, however a large amount of new features only responded to a recurrent heat stress. The results reveal that the plant's response to recurrent heat stress differs from its response to isolated heat stress, suggesting a memory effect in sorghum and irreversible impact of the stress on seed metabolism.

Poster P 26

Métabolomique urinaire et apprentissage automatique pour le suivi longitudinal des réponses physiologiques à l'entraînement en altitude chez des rameurs d'élite

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L'entraînement en altitude est devenu un pilier de la préparation des athlètes de haut niveau, permettant des adaptations supplémentaires, notamment respiratoires, hématologiques et métaboliques. L'exploration de ces changements par la métabolomique semble pertinente pour obtenir des informations plus détaillées.

Vingt-sept rameurs d'élite ont participé à un stage d'entraînement en altitude de 12 jours à 1850 mètres. Parmi eux, 18 ont terminé le stage sans problème de santé et ont été inclus dans les analyses ultérieures. Des échantillons urinaires ont été prélevés chaque matin et analysés par Résonance Magnétique Nucléaire. Des modèles d'apprentissage automatique (PLS-DA, LightGBM et XGBoost) ont été utilisés pour discriminer les échantillons entre le premier, le quatrième et le douzième jour. Enfin, nous avons prédit l'évolution de la créatinine, identifié comme discriminante entre les jours, à l'aide d'un réseau de neurones LSTM.

Les performances de l'ensemble des modèles ont permis de distinguer qualitativement les jours, avec une précision atteignant 93 %. Les variables discriminantes (VIP) et les valeurs SHapley Additive exPlanations (SHAP) se sont révélées cohérentes d'un modèle à l'autre, démontrant la complémentarité des approches. Le modèle de régression a également montré des résultats satisfaisants, avec un R2 de 0,61, en s'appuyant sur des prédictions issues des données métabolomiques et d'entraînement.

En conclusion, nous avons observé des adaptations métaboliques spécifiques au fil du temps en hypoxie et montré la complémentarité entre les modèles classiques PLS-DA et les méthodes plus avancées d'apprentissage automatique. Ce travail nous a également permis de développer un modèle de réseau de neurones prédisant leurs évolutions.

Poster P 27

Exposition aux micropolluants alimentaires : bioaccessibilité et métabolisation des pesticides polaires à l'aide d'un modèle intégré LC-HRMS / organe-sur-puce

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Le projet ExpoMicroPol vise à caractériser l'exposition humaine aux pesticides et métabolites polaires via l'alimentation, dans une démarche Exposome/One Health. Parmi ces composés, le desphényl-chloridazone (DPC), métabolite de la chloridazone, est l'un des plus fréquemment détectés dans les eaux potables en France. L'approche combine spectrométrie de masse haute résolution (LC-HRMS) et modèles organe-sur-puce foie. L'exploitation des données s'appuie sur un workflow bio-informatique pour l'identification des métabolites (MetID), combinant le prétraitement sous MS-DIAL, l'annotation structurale via SIRIUS, et l'automatisation par scripts R.
Cette étude se concentre sur la métabolisation de la chloridazone (CDZ), un herbicide dont les métabolites polaires sont fréquemment détectés dans les eaux potables. L'acétaminophène (APAP) est utilisé comme témoin positif de métabolisation. Les hépatocytes ont été exposés pendant 24h et 48h, et les surnageants analysés par LC-HRMS.

Les résultats confirment la métabolisation de l'apap par les hépatocytes, avec l'identification de deux métabolites majeurs : l'apap-glucuronide et le 3-hydroxy-apap. Concernant la chloridazone, les analyses montrent un effet métabolique étendu, surtout après 48h d'expositions. Sur le plan biologique, aucune toxicité cellulaire n'a été observée pour les deux composés aux concentrations testées (10µm).
Ces résultats démontrent la capacité du modèle hépatique sur puce à reproduire les voies de métabolisation connues (APAP) et à explorer le devenir de contaminants environnementaux CDZ. Le couplage avec les outils bio-informatiques permet une annotation rapide et fiable des métabolites, ouvrant des perspectives pour l'étude de l'exposome alimentaire et l'évaluation des risques liés aux micropolluants.

Poster P 28

Tomato 2100: From Stress to Shelf Life by Cracking the PLP-Ascorbate Code for Climate-Resilient Tomatoes

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Climate change is expected to intensify the frequency, duration, and severity of abiotic stresses such as heat waves and drought. Estimates of 22–79% tomato yield losses by 2100 reflect how climate driven stresses cause development and reproduction impairments, ultimately threatening global food production. Such stress induced penalties are tightly linked to disruptions in cellular redox homeostasis as environmental constraints induce excessive production of reactive oxygen species (ROS), which accumulate when antioxidant systems are overwhelmed, leading to oxidative damage.
Among plant antioxidants, ascorbate (vitamin C) plays a central role in detoxifying ROS and maintaining redox balance. Its metabolism is highly dynamic, involving multiple interconnected processes: (i) synthesis through several pathways, predominantly the L-galactose route where GGP acts as the key regulatory enzyme; (ii) recycling via the ascorbate–glutathione cycle, which regenerates reduced ascorbate from its oxidized forms; and (iii) degradation into threonate, oxalate or tartrate. These pathways intersect with central carbon metabolism and cell wall biosynthesis, highlighting the integration of ascorbate metabolism within broader cellular processes.
This project aims to elucidate how plants regulate ascorbate metabolism in response to environmental signals, with a particular focus on PAS/LOV photoreceptor proteins (PLPs), recently identified as protein level repressors of GGP, the key control point of ascorbate biosynthesis. Specifically, it aims to (1) uncover the biological functions of PLPs, (2) characterize the putative trade-off between ascorbate accumulation and plant growth or yield, and (3) determine how ascorbate enrichment influences stress tolerance and fruit shelf life, using tomato as a model crop.

Poster P 29

Unlocking the LRMS bottleneck through QC-Based HRMS enrichment for oxidation product identification

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Comprehensive annotation of oxidation products formed during plant-based food processing remains a major analytical challenge. In apple juice, these newly formed compounds exhibit distinct chemical properties compared to native metabolites and contribute to organoleptic quality, yet they remain poorly characterized.
Metabolite annotation is a major bottleneck in untargeted metabolomics, particularly when data are acquired using low-resolution mass spectrometry (LRMS). We propose a methodological strategy to enrich LRMS datasets with high-resolution mass spectrometry (HRMS) information based solely on the injection of pooled quality control (QC) samples.

The study model relies on controlled oxidation kinetics of apple juice (six independent replicates, 13 oxidation levels), generating 78 samples analyzed by UHPLC–DAD–LTQ XL (ESI–, full scan with data-dependent acquisition) using a metabolomics-compliant batch design including distributed pooled QCs. Only the pooled QCs were subsequently re-injected using UHPLC–DAD–Orbitrap Exploris 480 (ESI–, full scan with data-dependent acquisition) under harmonized chromatographic conditions to facilitate inter-platform alignment.

A QC-based LRMS/HRMS matching pipeline was developed using sequential filters based on retention time, nominal (or 0.1 Da) m/z, and MS2 spectral similarity. HRMS-derived information was then propagated to corresponding LRMS features.

This strategy enables improved deisotoping, assignment of accurate masses and molecular formulas, and enhanced annotation capacity while minimizing HRMS instrument time. This proof-of-concept provides a practical framework for hybrid LR/HR metabolomics workflows and optimized HRMS resource allocation.

Poster P 30

Spatial metabolomics on plant samples by Droplet Probe/ LC/HRMS – parameters to consider for this in-depth analysis

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The SepQuant Droplet Probe system is designed for in situ analysis of specialized metabolites on biological surfaces and works in conjunction with a QTOF-type UHPLC-HRMS for the separation and precise identification of compounds. Its principle is based on the automated deposition of a microdroplet of solvent onto the surface of the sample in order to extract metabolites locally and inject this extract into LC-HRMS for non-targeted DDA-type analysis. With a spatial resolution of less than 1 mm, the system allows precise sampling of different areas of the same organism as well as temporal monitoring of a living sample. It thus facilitates the study of interactions between plants, insects, and microorganisms, improves understanding of metabolic processes, and constitutes a major, innovative, and highly effective tool for spatial metabolomics in research. The implementation of this type of analysis requires the consideration of numerous parameters depending on the extraction conditions and the sample. Indeed, the shape of the drop and its spread at the liquid-sample junction depend on the solvent used and the volume of the drop on the one hand, and on the nature of the sample itself (impermeable, absorbent) on the other. Our method has been validated (linearity, repeatability, etc.) on model and real surfaces. The technique has been applied and validated on various biological surfaces (co-cultured fungi, leaves, roots, etc.) allowing metabolite differentiation between various areas, tissues and genotypes.

Poster P 31

HoliHao : Holistic approach for the selection of native plants adapted to the phytoremediation of polluted areas on Hao atoll in French Polynesia

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Anthropic activities have led to significant soil contamination in Hao atoll (French Polynesia). To adress this environmental challenge, the HoliHao project is developing a holistic, in situ phytoremediation strategy adapted to tropical insular conditions. The approach integrates environmental chemistry, plant ecology, microbiology, and social sciences to identify effective and locally adapted remediation solutions while preserving biodiversity.
An initial field campaign enabled the collection of seven indigenous plant species from both contaminated and control sites, along with rhizospheric and bulk soils for comparison. Untargeted metabolomics analyses (GC-HRMS, LC-HRMS) and metal analyses (ICP-MS) confirmed high levels of organic pollutants, including polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs), as well as metal contamination (e.g., Cu, Pb, Zn).

Preliminary observations suggest that three plant species (*Heliotropium foertherianum*, *Scaevola taccada*, and *Triumfetta procumbens*) may have phytoremediation potential. Ongoing field campaign aims to refine the selection of these key candidate species, with more replicates to verify these preliminary findings. Analyses of plant tissues are currently underway to investigate pollutant accumulation and potential biodegradation processes.
Overall, this work provides a framework for nature-based, locally acceptable remediation strategies in tropical island environments, combining scientific innovation with strong societal integration.

Poster P 32

EMF : Suivi de la dissipation et de l'impact écologique d'un biopesticide, de l'extrait à la formulation complète

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Face aux préoccupations croissantes concernant l'impact des pesticides sur l'environnement et la santé humaine, les biopesticides issus de sources naturelles, telles que les plantes ou les micro-organismes, apparaissent comme des alternatives prometteuses. Ces produits sont toutefois des mélanges complexes, comprenant substances actives, constituants de l'extrait biologique et coformulants, souvent négligés dans les études. Cette complexité complique les études de leur suivi environnemental et de leurs produits de transformation.
Contrairement aux pesticides conventionnels, dont l'analyse se limite souvent à quelques molécules cibles, les biopesticides requièrent des approches analytiques globales. L'Environmental Metabolomic Footprinting propose une approche cinétique de profilage en métabolomique non ciblée permettant d'étudier l'évolution du métamétabolome de microcosmes de sol traités par ces produits complexes et de définir un temps de dissipation.
L'entreprise AKINAO a développé un biofongicide à base d'extrait d'inule visqueuse, efficace contre le champignon Monilia laxa, qui affecte les arbres fruitiers. Une étude cinétique a été menée sur neuf pas de temps afin d'estimer la dissipation de l'extrait non formulé, de l'extrait formulé et de la formulation blanche. Le profilage métabolomique par HPLC-HRMS a été réalisé sur des sols traités et un sol non traité, avec cinq réplicats biologiques. Les résultats montrent une disparition complète de la substance active complexe en six jours, tandis que certains composés de la formulation persistent au-delà de 127 jours. L'approche métabolomique permet d'approfondir l'analyse en évaluant les effets de ces substances sur la biodiversité du sol, constituant ainsi un outil fiable pour évaluer l'impact environnemental des biopesticides.

Poster P 33

Exploring combination of CID/EAD fragmentation to improve structural annotation of freshwater microbial metabolome in UPLC-HRMS/MS-based untargeted approach

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Structural annotation remains one of the most challenging tasks in untargeted metabolomics as 2-20% remains being considered as metabolic "dark matter". To tackle this challenge, the last years have seen the unprecedent development of new fragmentation method such Electron Activated Dissociation (EAD) and bio-informatic solutions including machine/deep learning-based tools and molecular network-based approaches. Among new fragmentation, EAD has recently demonstrated its ability to provide complementary information to usual CID/HCD approaches, especially for lipids annotation. Concomitantly, SIRIUS is exponentially used for in silico structural elucidation of known and unknown chemicals while MSnet proposes to propagate annotation by using structural-similarity based-network. The present study aims to explore the added-value of EAD fragmentation combined to cutting edge bioinformatic pipelines to unlock aquatic microbial ecosystem metabolome. To do so, EAD and CID spectral library of almost 3000 metabolites is under development based on various fragmentation energies and chromatographic separation (C18, HILIC) by using IROA libraries and additional in house specialized metabolites from plants and micro-organisms. The metabolome of individual species of diatoms, cyanobacteria, green-algae and more complex communities will be explored by using this new library and further implementation of SIRIUS and MSnet tools on EAD fragmentation spectra to provide a more comprehensive picture of the microbial biochemical diversity.

Poster P 34

Redox imbalance and male sterility in tomato

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Climate-driven heat stress is emerging as one of the most severe constraints on global crop productivity, largely because of the extremely sensitivity of reproductive development, possibly linked to redox balance and hormone signalling . In tomato, we previously found that excessive accumulation of ascorbate, the central antioxidant of plant cells, leads to male sterility, highlighting a redox-dependent vulnerability that might be highly relevant under future climatic scenarios. Yet the metabolic disruptions and spatial redox shifts underlying this phenotype remain poorly characterized.

To investigate these processes, we performed targeted and untargeted metabolomics on tomato plants engineered to accumulate high ascorbate levels. Elevated ascorbate led to a marked reduction in abscisic acid (ABA), consistent with transcriptomic signatures of attenuated ABA pathways, and altered metabolites essential for reproductive success, including dicoumaroyl spermidine, required for pollen germination and tube growth. Spatial analysis using MALDI mass spectrometry imaging revealed a strong enrichment of putative NADP-related ions in stamens, particularly within pollen sacs, indicating localized redox perturbations in male reproductive tissues.

Building on these MALDI-MSI results, we will next apply DESI imaging as a complementary approach. DESI's ambient ionization and minimal sample preparation make it particularly suitable for detecting fragile redox cofactors and small metabolites that may be difficult to preserve with MALDI. This additional imaging modality will refine our spatial understanding of redox–hormone interactions driving heat-induced sterility.

Poster P 35

Metabolomics Strategy Using Cost-Effective Capillary Electrophoresis (Pharmelp) to Assess Quality of Anti Inflammatory Herbal Products

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Nowadays, the widespread use of natural products to treat certain types of diseases is still the gold standard, especially in developing countries. These products are often subject to adulteration or falsification, making herb testing essential to address to the population good quality products.
Through a partnership with Pharmelp (a swiss non-profit organization), we have access to a cost-effective and low-tech device of capillary electrophoresis. We are focusing on developing analytical strategies to study herbal medicinal products in the footsteps of Serge Rudaz team who works on drug falsification(1). As a first step, we have chosen three plants and analyzed 17 food supplements for the treatment of articulation pain.

The bioactive compounds found in the rhizome of turmeric (*Curcuma longa* L.), in devil's claw (*Harpagophytum procumbens* (Burch.) DC. ex Meisn.) and in the root of scrophularia (*Scrophularia nodosa* L.) have been analyzed. Indeed, curcuminoids (in turmeric) and the glycoside harpagoside (in *Scropholaria* and *Harpagophytum*) play a key role in counteracting inflammatory conditions affecting the joints.

An untargeted metabolomic strategy has been undertaken to compare different herbal food supplements. Calibration curves have been established on main bioactive compounds standards and the latter have been quantified in the herbal products.

This work demonstrates that cost-effective capillary electrophoresis constitutes an appropriate strategy to mitigate unresolved bottlenecks in analytical instrumentation for herb quality control in developing countries.

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Poster P 36

Optimization of metabolite identification in NMR-based metabolomics using standard mixtures and spike-in strategies

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NMR-metabolomics is widely used for the analysis of complex biological matrices due to its robustness, reproducibility and minimal sample preparation. However, signal overlap in ^{1}H NMR spectra remains a major limitation, leading to ambiguous annotations and reduced analytical performance. The use of 2D NMR experiments improves signal dispersion along a new dimension and facilitates metabolite identification. UF and NUS fast 2D NMR strategies make them applicable to metabolomics studies by reducing acquisition time. This work focuses on the metabolite identification step of 1D ^{1}H NMR and fast 2D NMR metabolomics workflow. The main objective was to apply a reliable identification approach to a metabolomics study of pig serum samples exposed or not to bisphenol A. Complete annotation of quality control samples 1D (^{1}H) and fast 2D NMR (UF COSY, NUS zTOCSY, NUS HSQC) spectra was performed and 52 metabolites were annotated. Optimized standard mixtures were then designed to minimize the number of spiked samples and experiments. These mixtures were constructed using a custom R Shiny application by grouping compounds with non-overlapping signals. The four NMR experiments were recorded on the mixtures of standards and exploited to validate the initial annotations. To obtain a level 1 identification, spike-in experiments were performed, using the optimized mixtures of standards. The resulting targeted signal intensity enhancement allowed robust validation of numerous metabolites while reducing the number of spike-in experiments and limiting false positives. Ultimately, the data will be organized for further import into the MetaboHub shared database PeakForest for future metabolomics studies.

Poster P 37

Unveiling interaction-driven metabolite production in four fungi from Prorocentrum lima phycosphere

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Marine fungi are a chemically rich, underexplored source of novel natural products. Despite numerous attempts to produce specialized metabolites in laboratories, genome studies have shown that a significant proportion of biosynthetic gene clusters remain transcriptionally silent under standard laboratory culture conditions. This discrepancy between genomic potential and observed metabolite production highlights a major obstacle in the discovery of microbial natural products. Co-culture strategies have emerged as a promising approach for mimicking ecological interactions and triggering cryptic biosynthetic pathways (Arora et al., 2020, 10.1016/j.biotechadv.2020.107521). Using interspecies chemical communication and competitive stress, microbial co-cultivation can activate silent gene clusters, resulting in the production of previously undetected specialized metabolites.
Our goal is to demonstrate how ecological interactions can be used to reveal hidden chemical diversity and expand the range of microbial natural products through integrated metabolomic profiling by LC-HRMS. In this study, we investigate the co-culture of four fungi, coming from the same ecological niche (two Aspergillus and two Penicillium strains (Berry et al., 2023, 10.1111/1462-2920.16271)), in fifteen unique cultivation conditions with mono-, co-, tri- and tetra-culture. Metabolomics techniques were employed to identify co-culture induced metabolites using dedicated statistical methods (such as Projected Orthogonalized CHemical Encoutered MONitoring approach (Jansen et al., 2015, 10.1007/s11306-014-0748-5)) that were expanded to multi-culture.

This study demonstrates the complexity and specificity of fungal-fungal interactions and identify unprecedent specialized metabolites that need to be elucidated. Acknowledgments: Financial support was provided by the French National Agency (ANR-25- CE20-3137; HoloFungi project) and the Joint Master Aquaculture Environment and Society (ACES+).

Poster P 38

High-Throughput Metabolomics: Decoding Plant-Microbiome Chatter

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Plant-associated microbiomes play a central role in plant adaptation, growth, and resistance to biotic and abiotic stresses. While recent studies have highlighted the ability of plants to modulate their microbiome in response to pathogen attack, the mechanisms underlying this "cry-for-help" remain poorly understood to date.

The MicroHelp project aims to elucidate the metabolic and microbial dialogues between rice (Oryza sativa), a major global food crop, and three types of foliar pathogens (viruses, bacteria, fungi) with contrasting agronomic impacts.
To finely characterize these interactions, we have established an analytical workflow based on a high-throughput robotic extraction method from soil to analyse root exudates, enabling metabolomic analysis with liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS).

Our preliminary results reveal a rapid and specific response of root exudates as early as two weeks post-inoculation, suggesting a differential response of rice depending on the pathogen type. These data, combined with microbial diversity analyses, open up concrete applications in microbiome engineering and varietal selection to enhance crop resistance and reduce the use of pesticides. This approach, at the interface of metabolomics, microbiology, and bioinformatics, offers innovative perspectives for the development of sustainable crop protection strategies, particularly for rice, whose production is crucial for global food security.

Poster P 39

An Energy-Based Perspective for Evaluating Metabolic Network Coverage

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Untargeted metabolomics often fails to capture all metabolites due to the vast, diverse chemical space of small molecules, which leans on condition-dependent analytical methods such as LC-MS, leading to a high volume of ambiguous features that lack corresponding, high-confidence matches in incomplete reference databases. Current methods for assessing metabolome coverage do not effectively differentiate metabolites in related biochemical pathways from those in unrelated processes. To address this, we propose a physics-based energy formulation tailored to metabolic networks to evaluate the trade-off between local and global coverage. This approach provides a topological metric for assessing metabolic network coverage and the impact of different analytical workflows in mass spectrometry. The resulting metric quantifies coverage based on the information content and completeness of metabolite observations and can guide method selection to enhance the biochemical representativeness of data.

Poster P 40

One network to link them all: Integrating LC-MS data for deeper metabolite coverage

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Metabolomics aims to cover a large range of metabolites from polar metabolites to hydrophobic lipids. Therefore, multiple chromatographic methods – such as reversed phase chromatography (RPLC) or hydrophilic interaction chromatography (HILIC) – are combined to obtain a comprehensive overview. Resulting tables need to be combined afterwards for data analysis, but several metabolites might be detected across multiple methods. Currently, it is only possible to deal with such multiple entries for identified metabolites. There is a strong requirement for data fusion strategies beyond simple concatenation of individual peak tables. Networks have been shown to represent a powerful tool for metabolomics data analysis. Feature-based molecular networking or ion identity networking are modern tools to reconstruct biochemical knowledge from metabolomics data.

Here developed a molecular network across multiple acquisition methods for a more comprehensive combination of data and metabolites identification. MS/MS spectra between the different LC-methods datasets were compared to merged features together. Within single chromatographic methods, ion mode matching based on predefined adducts were used to identify metabolites. Within single ionization modes, spectra were match based on GNPS mass-shift cosine similarity. A large network was generated based on the different connections.

The network was tested on several blood-related matrices. Analysis were performed using RPLC-MS for mid- to non-polar metabolites and HILIC-MS for polar metabolites. Identification was performed using in-house and external spectral libraries, as well as prediction software such as Sirius. Well-known metabolites detected in all tested analytical methods, such as tryptophan, were successfully connected. Data was then mined for new metabolites and associations.

Poster P 41

Metametabolome insight in the structural, physiological and adaptative responses of freshwater periphytic communities to natural fungicides

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Facing increasing environmental and human health concern about synthetic pesticides, biopesticides have been proposed as a less hazardous alternative. Unfortunatly, there is still paucity of knowledge about their actual effect and tolerance of non-target species, such as microbial communities playing a pivotal role in ecosytems functions and associated services. To address this gap, meta-metabolomics can provide a comprehensive picture of the molecular/biochemical phenotype of microbial communities complementary to usual descriptors at the structural and physiological levels. This study aims to elucidate the responses and tolerance mechanisms of periphytic microbial communities exposed to the natural biocides kasugamycin, copper and their mixture. To do so, an untargeted metabolomic approach based on LC-HRMS/MS was combined with physiological (photosynthetic, heterotrophous enzymatic activities), structural (biomass, algal composition) and adaptive (Pollution-Induced Community Tolerance) descriptors to assess the community response along a 28-day chronic exposure. At the structural level, kazugamicin triggered a significative increase of the phototrophs biomass while copper led to an increase of diatoms and decrease of green algae. At the physiological level, the photosynthetic activity was inhibited by the highest concentration of kazugamicin while copper trigger an decrease of enzymatic activity. In terms of adaptation, both biocides led to a transiant tolerance acquisition. Finally, metametabolomic analysis revealed significant effects of both time, kasugamycin and copper on the community metabolism. Altogether, these results will contribute to elucidate the cascade of events leading to response and further tolerance of microbial communities (i.e. eco adverse/tolerance outcome pathways) to natural biocides.

Poster P 42

Metabogène : vers un nouvel outil d'annotation pour explorer la diversité biochimique de produits naturels du lin (*Linum usitatissimum* L.)

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Les plantes constituent une source majeure de molécules bioactives, produisant une grande diversité de composés aux propriétés chimiques et biologiques variées. Toutefois, leur identification reste longue en raison des étapes de fractionnement bioguidé nécessaires avant une caractérisation complète par résonance magnétique nucléaire (RMN) et spectrométrie de masse haute résolution (HRMS).

Dans ce contexte, nous développons une preuve de concept d'un outil d'annotation innovant combinant données analytiques (LC-HRMS) et approches génomiques de type mQTL afin d'accélérer l'identification des métabolites. Des travaux récents menés au sein de l'UMRT BioEcoAgro INRAE 1158 ont mis en évidence, chez le lin (*Linum usitatissimum* L.), des corrélations entre marqueurs génétiques et accumulation de métabolites structurellement proches. A partir d'une population de lignées recombinantes (RILs) issue du croisement entre un lin d'hiver et un lin de printemps, nous avons regroupé des métabolites partageant à la fois des régions génomiques communes et des similarités structurales avec un niveau de précision inédit. L'approche permet notamment de distinguer les flavones di-glycosides dérivées de l'apigénine de celles issues de la lutéoline, démontrant ainsi la capacité du modèle à discriminer des composés ne différant que par leur aglycone. Elle différencie également les flavones selon leurs modifications (méthylation, glycosylation) et selon la nature et la position des résidus glycosidiques (O- ou C-). Au-delà des flavones, des regroupements spécifiques ont été observés pour les cyanogènes, lignanes et dérivés d'acides hydroxycinnamiques.

En cours d'optimisation, ce modèle d'annotation contribuera à accélérer l'exploration du métabolome du lin et à terme orienter l'élucidation des voies de biosynthèse.

Poster P 43

Réponses métaboliques précoces et retardées après exposition à un mélange représentatif de produits de combustion de propergols solides : complémentarité LC-MS/^{1}H-RMN

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De récentes études ont démontré que la combustion des propergols de fusées et missiles pouvaient générer des aérosols associant nanoparticules d'alumine (NPs AlO) et du chlorure d'hydrogène gazeux (HClg), mais leur toxicité reste peu documentée. L'exposition des personnels se fait principalement par inhalation, et pourrait, après plusieurs itérations, induire une toxicité systémique. Cette étude visait à évaluer, via une approche métabolomique non ciblée, les impacts d'une telle exposition en fonction de la dose et du temps.

Des rats Wistar mâles ont été exposés 4 heures par jour pendant 4 jours à de l'air (contrôle) ou à un mélange de polluants (HClg à 5 ppm et NPs AlO à 1, 5 ou 20 mg/m^3). Des échantillons sériques ont été prélevés aux jours 1 et 28 post-exposition et analysés par UPLC-QToF (full scan MS et DDA pour l'identification) en phase inverse et HILIC, en mode d'ionisation positif et négatif. Une approche complémentaire par ^{1}H-RMN a été effectuée. L'exploitation des données a été réalisée avec MetaboAnalyst.

Aucun effet dose-réponse n'a été observé, ni au temps précoce (jour 1) ni au temps tardif (jour 28). Cependant, une perturbation métabolique a été détectée dès le jour 1 à la dose maximale (20 mg/m^3) par LC-MS. Au temps tardif, des altérations métaboliques sont apparues à la dose intermédiaire (5 mg/m^3), à la fois en LC-MS et en ^{1}H-RMN. Ces résultats suggèrent l'existence de réponses métaboliques précoces et retardées, dont la détection varie selon la plateforme analytique, soulignant ainsi la complémentarité des approches métabolomiques.

Poster P 44

Metabolomic workflow for oxidative post-translational protein modification identification: a case study for oxidized LDLs

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Oxidative modification of low-density lipoproteins (LDLs) is a central mechanism driving the early stages of atherosclerotic plaque formation. Particular attention has been given to the role of myeloperoxidase (MPO). In vivo, this enzyme is present in the atheromatous plaque and produces hypochlorous acid (HOCl) from hydrogen peroxide (H2O2) and chloride ions (Cl–). HOCl is a oxidant that can modify both LDL lipids and the apoB-100 protein. However, LDL oxidation mediated by the MPO–HO–Cl system leads to more selective protein modifications that are not reproduced by direct HOCl treatment. In this context, the aim of this study was to generate and compare LDLs oxidized under different conditions to characterize their molecular signatures. To investigate these differences, trypsinized LDL ApoB-100 and peptides were injected by RP-LC-HRMS. The datafiles were converted in ".xml" files and analyzed with W4M workflow adapted for peptide analysis. The datasets were analyzed using multivariate statistics, revealing substantial overlap between LDLs oxidized under different conditions, indicating limited global metabolomic differences. However, patterns varied by oxidation system. Mild conditions (HO and MPO with lower HO concentration) showed high intra-group variability and poor clustering, suggesting heterogeneous, less reproducible modifications. In contrast, stronger conditions (HOCl and MPO–HO–Cl with higher HO concentration) produced clearer group separation, indicating more consistent and potentially specific molecular signatures. Overall, while LDL oxidation may converge toward common end products, the type and intensity of the oxidizing system affect the reproducibility and specificity of the resulting modifications, warranting further study.

Poster P 45

Molecular Networking for stability monitoring of cosmetic complex mixtures

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Introduction Ensuring product stability and safety is critical in the cosmetic industry. Non-targeted LC-HRMS analysis, combined with Molecular Networking (MN) for tandem mass spectra visualization, is a key asset for prioritizing annotation of unknown transformation products. This study compares three platforms-Ometa Labs (OL), Compound Discoverer (CD), and MetGem (MG)-using a natural extract and two cosmetic formulas subjected to degradation stress. Methods Acquisitions were performed on an Orbitrap Fusion HRMS with an UltiMate 3000 UPLC (Thermo Fisher Scientific). ESI parameters: 3850V(+)/3500V(-) spray voltage, nebulization gas 30 AU, auxiliary/sweep gases 5 AU, transfer tube at 325◦C, and vaporization at 400◦C. DDA (top 3) and DIA (20 m/z isolation window) used HCD at 25% stepped NCE in non-resonant mode. Data were processed via FreeStyle (v4.4) and Compound Discoverer (v3.3) using mzCloud and in-house mzVault databases. Ometa Labs was utilized for MN visualization. Results A benchmark of MN tools (data conversion, construction, and querying) led to the selection of OL, CD, and MG. Metabolites were annotated using dereplication and de novo characterization. Redundancy was reduced through OL's feature-based workflow and CD's DIA datasets, while MG's tSNE projection enhanced chemical mapping. Node-integrated pie charts represented ion abundance evolution under stress (time/temperature). This relative comparison, coupled with cluster annotation, enabled rapid prioritization of nodes of interest. Consequently, the stability of actives, ingredients and excipients can be assessed to provide robust formulation guidelines. Impacts/Novelty This work provides methodological insights into MN applications and pragmatic data to ensure the stability of complex cosmetic formulas.

Poster P 46

Combining AcquireX™ data acquisition and Feature-Based Molecular Networking approach to deeply explore oxidation markers of condensed tannins

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The significant role of condensed tannins (CTs) in various fields has encouraged many researchers to investigate these compounds. Indeed, this class of polyphenolic compounds contributes to the quality of various foods and fruits-derived beverages and possesses antioxidant properties, important in preventing chronic diseases such as cancer and neurodegenerative disorders. Advances in analytical tools using mass spectrometry have greatly enhanced the exploration of complex metabolites using high throughput approaches such as Feature-Based Molecular Networking (FBMN).

In this study, to overcome the challenges of finely characterizing CTs and their chemical evolution, FBMN approach was combined with a thioglycolysis and an MS/MS data acquisition using AcquireX™ Deep Scan workflow, on the High-Resolution Mass Spectrometer Orbitrap Exploris 480. This workflow employs an advanced iterative data acquisition strategy that dynamically optimizes precursor ion selection in real-time. Its continuously refines exclusion and inclusion lists between sample injections, significantly enhancing the depth and quality of MS analysis. The system efficiently manages overlapping m/z values by evaluating relative ionic intensity ratios between blanks and samples. This increases compound detection and achieves scan rates of up to 40 Hz, ensuring high-quality fragmentation spectra.

Through this methodology, applied to grape seeds, a rich source of CTs, AcquireX™ tripled the number of unique and exploitable fragmentation spectra, yielding approximately 950 MS/MS spectra compared to approximately 300 for a ddMS2 acquisition. 104 oxidation markers were highlighted, including 49 previously unreported. These findings enhance understanding of the structural evolution of CTs, which significantly impact the quality and the stability of products containing them.

Poster P 47

Untargeted multimodal mass spectrometry for the characterization of oenological extracts rich in gallotannins

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Gallotannins are hydrolysable tannins composed of gallic acid units esterified to a polyol core, most commonly glucose, and exhibit high structural diversity with varying degrees of polymerization. Gallnut-derived extracts rich in gallotannins are widely used in winemaking to stabilize wine color, improve must and wine clarification, promote partial protein precipitation, and enhance antioxidant protection. Previous liquid chromatography–mass spectrometry (LC-MS) studies have revealed substantial compositional variability among commercial gallotannin extracts, but their chemical composition remains insufficiently characterized due to high structural complexity and extensive isomerism.

The aim of this study was to improve the characterization of gallotannin extracts from our internal collection using untargeted and multimodal mass spectrometry (MS) approaches. Analyses were performed on two high-resolution mass spectrometers (Orbitrap Exploris 480 and timsTOF Pro2), providing orthogonal and complementary information. Three analytical strategies were combined: Kendrick mass defect (KMD) analysis to visualize homologous galloyl series, ion mobility spectrometry (IMS) to resolve isomeric species, and molecular networking (MN) to explore structural relationships among detected compounds.

KMD analysis proved highly effective for rapid visualization of gallotannins in MS data, while IMS enabled the detection of previously unreported isomeric species. The combined use of KMD, IMS, and MN allowed the annotation of numerous gallotannins with molecular weights ranging from approximately 330 to 3000 Da and revealed chemical differences among extracts. This study highlights the strong potential of multidimensional MS for the in-depth analysis of complex polyphenolic mixtures, the selection of oenological gallotannin extracts, and the characterization of gallotannins from other food and plant sources.

Poster P 48

Comparaison des métabolomes urinaire, sanguin et salivaire et de leurs variations à la suite d'un évènement contrôlé

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La métabolomique suscite un intérêt croissant, notamment en médecine personnalisée. Si le plasma/sérum demeure la matrice de référence, son caractère invasif encourage l'exploration de biofluides alternatifs moins contraignants, tels que l'urine et la salive, particulièrement adaptés à l'auto-prélèvement pour le suivi des patients. Dans ce contexte, nous avons comparé les variations métabolomiques de ces matrices en conditions dynamiques.
14 volontaires (7 hommes et 7 femmes) ont été soumis à une prise alimentaire suivie d'une activité physique contrôlée. Des échantillons sanguins, urinaires et salivaires ont été collectés à 3 temps de prélèvement : à jeun (T1), après prise alimentaire et activité physique (T2) et à jeun une semaine après (T3). Les profils métabolomiques ont été obtenus par RMN 1H 500 MHz. Après quantification et bucketing, la sélection de variables par analyses multivariées a permis d'obtenir des modèles présentant des séparations comparables entre les groupes dans les 3 biofluides.

Les analyses univariées ont ensuite identifié 12 métabolites significatifs dans le sérum, 14 dans la salive et 45 buckets urinaires, contribuant aux variations entre les conditions sans (T1 et T3) et avec (T2) évènement. L'exploration des voies métaboliques a révélé une concordance partielle, avec 4 voies communes aux matrices : cycle de Krebs, métabolisme de la proline et arginine, du glycoxylate et dicarboxylate, et de l'alanine, aspartate et glutamate. Ces résultats soulignent la complémentarité des 3 biofluides, tout en confirmant qu'ils ne sont pas interchangeables. Toutefois, pour certains métabolites présentant des variations concordantes, l'urine et la salive pourraient constituer des alternatives intéressantes au sang.

Poster P 49

Effet d'un régime riche en amidon lentement digestible sur les systèmes métaboliques de patients diabétiques de type 2

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Cinquante-et-un patients atteints de diabète de type 2 (âge=62, IMC=30,4 kg/m^2, HbA1c=7,2 %) ont suivi 12 semaines de régime riche (H-SDS) ou pauvre (L-SDS) en amidon lentement digestible basé sur le choix et la cuisson de féculents du commerce. Le régime H-SDS a réduit la variabilité glycémique et l'HbA1c, améliorant le contrôle glycémique. Nous avons cherché à compléter ces observations en évaluant l'effet du régime sur l'organisation des systèmes métaboliques.
Les métabolites plasmatiques ont été extraits et analysés par LC-HRMS/MS (Orbitrap Exploris 240) et les données spectrales prétraitées avec MS-DIAL. Deux-cent-quatre-vingt-neuf métabolites ont été annotés et regroupés en environ 40 unités fonctionnelles. L'impact des régimes a été évalué à l'échelle de ces unités plutôt qu'au niveau des métabolites individuels. Les onze unités affectées par les régimes (approche PLS) ont été déclinées en amont en voies biochimiques et en aval en modules du système biologique. Ces trois niveaux d'information (biochimique–fonctionnel–système) ont été intégrés dans un graphe de connaissances représentant le système métabolique sensible aux régimes.

L'analyse topologique du système métabolique a révélé un noyau structuré autour de trois fonctions majeures : métabolisme du microbiote, métabolisme des glucides et rééquilibrage de désordres métaboliques principalement liés aux acides aminés à châine ramifiée. Les voies du fructose et du mannose ainsi que celle de la glycine, sérine et thréonine occupent une position carrefour reliant ces fonctions.
En conclusion, l'analyse métabolomique déclinée selon une approche systémique multi-niveaux (biochimique–fonctionnel–système) met en évidence un noyau de régulations métaboliques associé aux effets des régimes.

Poster P 50

Novel sample preparation for the pre-treated biomass characterization using MALDI-FTICR

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The study of lignocellulosic biomass carried out as part of the Amaretto project (France 2030, PEPR B-BEST), aims to identify molecular markers and predict the reactivity of biomass for bioethanol production. To this end, the solid fraction of pretreated lignocellulosic biomass, which presents significant analytical challenges due to its heterogeneity, is characterized.
A key challenge lies in preparing homogeneous solid samples suitable for laser ablation. Biomass pellets are therefore produced, with or without matrix addition, and analyzed using Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FT-ICR, SolariX XR 9.4T) coupled with a Matrix-Assisted Laser Desorption/Ionization (MALDI) ion source.

In negative ion mode, Laser Desorption/Ionization (LDI) approach enables direct molecular fingerprinting without prior chemical treatment. Complementary MALDI experiments using various matrices, were conducted to explore additional ion formation and enable internal calibration. Optimization of instrumental parameters ensured sub-ppm mass accuracy over anm/z range of 100–700, allowing reliable elemental formula assignments. The resulting spectra are dominated by radical and deprotonated CxHyOz species with hundreds of ions annotated per sample. Van Krevelen diagrams provide detailed insights into the molecular composition of the solid biomass fraction.

In positive ion mode, LDI/MALDI-FTICR analyses extend molecular coverage toward highermass species. Method development focuses on optimizing matrix selection, concentration, and deposition to enhance ion generation, ionization efficiency, and overall signal quality. These results highlight the complementarity of LDI and MALDI-FTICR approaches for comprehensive biomass characterization. Future work will focus on multivariate statistical analyses to correlate molecular signatures and biomass reactivity.

Poster P 51

Advancing Spatial Metabolomics: Semi-Quantitative Mapping via Targeted DESI-QqQ and Internal Standard Spraying

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Mass spectrometry imaging (MSI) is an analytical technique that provides spatial information on molecular distributions within a sample. The combination of a Desorption ElectroSpray Ionization (DESI) source with a triple-quadrupole mass spectrometer (QqQ) is a recent improvement, enabling targeted metabolite imaging using Multiple Reaction Monitoring (MRM) transitions to reach higher sensitivity.
However, the absence of Total Ion Chromatogram (TIC) prevents signal normalization, thereby hindering both the comparison between tissue section analyses and the ability to monitor dysregulation over time.

Our objective is to develop a semi-quantitative DESI-QqQ imaging method to visualize the distribution of a set of metabolites. To enable comparison between tissue sections of brain mix, a solution of internal standards at known concentrations was sprayed onto the tissue surface prior to DESI analysis. This strategy allows the calculation of intensity ratios between targeted metabolites and their corresponding internal standards, enabling comparative analysis across different tissue sections and experimental conditions.

As a proof of concept, this approach was applied to rat brain. These results represent a first step toward robust relative quantification of targeted metabolites by DESI-MSI and offer promising perspectives for comparative and longitudinal studies.

Poster P 52

Is the contralateral cerebral hemisphere a relevant control for studying acoustically mediated BBB opening?

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Objectives : This study aims to determine whether acoustically induced BBBO in one striatum alters metabolic profiles in the contralateral striatum using multimodal metabolomics analytical approaches.

Methods : Male Sprague Dawley rats underwent acoustically mediated BBBO in the right striatum using focused ultrasound combined with intravenously injected microbubbles (MB-assisted US). Animals were sacrificed 3 hours, 2 days, or 1 week post-treatment. Ipsilateral and contralateral striata were collected following saline perfusion. Metabolites were extracted from lyophilized tissues and analyzed using 1H-NMR spectroscopy and HPLC–MS. Multivariate and univariate statistical analyses were applied to identify metabolic alterations and affected pathways.

Results : Evans Blue staining confirmed that MB-assisted US induced BBBO exclusively in the ipsilateral striatum. Metabolomic analyses of contralateral striata showed highly homogeneous metabolic profiles across control, 2-day, and 1-week groups, as evidenced by PCA. A transient shift was observed at 3 hours post-opening, although strong overlap persisted between groups and PLS-DA failed to generate predictive models. Univariate analyses identified 24 significantly altered metabolites, revealing transient disruptions in amino acid–related pathways. These included glycine, serine, and threonine metabolism, branched-chain amino acid biosynthesis, and lysine degradation. Only 3-hydroxykynurenine levels significantly decreased over time.

Conclusion : This study demonstrates that acoustically induced BBBO causes minimal and transient metabolic changes in the contralateral striatum, suggesting compensatory mechanisms. The findings emphasize the need for independent control groups and encourage further investigation of bilateral metabolic effects across distinct brain regions following acoustically mediated BBBO.

Poster P 53

Endocrin disruptor effect on trout larvae development and characterization of the metabolomic response

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Many synthetic chemicals used in agriculture and industry, classified as endocrine disruptors (EDs), are ubiquitous in aquatic environments. Fish embryos are particularly vulnerable to such compounds. While apical effects have been described at the morphological level, knowledge regarding their impact on the global metabolism of developing embryos remains limited. In this context, untargeted metabolomics represents a powerful approach, as it enables sensitive characterization of the molecular/biochemical phenotype alongside physiological descriptors. This study aims to characterize the effects of two EDs on the metabolism and physiology of rainbow trout (*Oncorhynchus mykiss*) embryos, a species of economic and ecological importance.
To achieve this, trout larvae were exposed daily for one month to sodium fluoride (1.5 and 5 mg/L), a potential ED used in industrial processes, and tebuconazole (20 and 100 µg/L), a well-established endocrine-disrupting fungicide widely applied in agriculture. Sampling was conducted at 8, 14, 20, 27 days of exposure. The metabolome was analyzed using an untargeted approach based on UPLC-HRMS-TOF. Data were processed with MZmine and analyzed using multivariate chemometric methods, including PCA, sPLS-DA, HCA, ASCA, and AMOPLS. Metabolite annotation was performed using SIRIUS and MSnet.

Physiological differences were observed, with embryos exposed to the highest concentrations exhibiting reduced standard length. Metabolomic profiles showed strong clustering driven by sampling time. ASCA and AMOPLS analyses indicated that time accounted for 43% of total variation, whereas ED concentration explained only 2.5%.

Overall, this study highlights the relevance of untargeted metabolomics for detecting metabolic disruptions induced by EDs during critical early developmental stages.

Poster P 54

Metabolomic and Lipidomic Insights into the Effects of Anticancer Drug Combination in Various Renal Cancer Models

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Subtherapeutic drug combinations are increasingly used in cancer therapy to reduce toxicity and limit resistance through synergistic interactions that selectively target multiple pro-cancer pathways. However, the molecular mechanisms underlying these interactions remain insufficiently characterized. Here, we investigated these mechanisms using untargeted metabolomics and lipidomics in clear cell renal cell carcinoma (ccRCC) models following exposure to a four-drug combination of tyrosine kinase inhibitors (erlotinib-HCl, dasatinib) and histone deacetylase inhibitors (tacedinaline, tubacin).To assess the cellular model's impact on the response to drug treatment, three ccRCC models of increasing complexity were used: 2D monolayers, 3D homotypic spheroids, and 3D heterotypic spheroids co-cultured with fibroblasts. After 48h treatment, global metabolomic and lipidomic profiling by high resolution mass spectrometry was performed using a zHilic (pH=9.3) and a C18 column, respectively, yielding 200 annotated metabolites and 700 lipids.

The models presented major differences, including increased triglycerides and ceramides and decreased phospholipids in 3D systems compared to 2D. Fibroblast co-culture further increased ceramide levels. Drug response differed across models, with lower efficacy in 3D models, especially in co-culture. The combination increased greatly ceramides and triglycerides, mainly driven by erlotinib-HCl/tubacin. As ceramides are pro-apoptotic, their accumulation likely contributes to cytotoxicity. Metabolomics revealed disturbed levels of key metabolites involved in sphingolipid metabolism, confirming lipidomics observations. The 3D models again displayed an attenuated effect, as higher baseline ceramide levels probably offer better buffering capacity.
Overall, these results highlight the value of metabolomics and lipidomics for elucidating drug mechanisms and the strong impact of cellular model evaluation on treatment response.

Poster P 55

Analytical evaluation of blood microsampling devices for home-based metabolomics and lipidomics studies

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Dried blood spot (DBS) sampling is widely used for neonatal screening and anti-doping testing and represents a promising approach for biomarker discovery studies. Blood microsampling devices are particularly attractive for large-scale clinical and epidemiological studies because they are minimally invasive, compatible with self-collection, and require only small blood volumes. However, conventional DBS devices such as cellulose-based cards may be affected by hematocrit-dependent bias and may not always ensure accurate volumetric collection, which can compromise analytical reproducibility.
Here, we evaluate the analytical performance of emerging blood microsampling devices, including volumetric absorptive microsampling and quantitative DBS, developed to improve blood volume accuracy and reduce hematocrit-related effects. Different extraction strategies, including metabolomics-, lipidomics-, and biphasic-oriented protocols, are assessed and coupled with HPLC-HRMS/MS analysis to identify workflows providing the broadest and most robust metabolic coverage.

Analytical performance is evaluated through complementary criteria reflecting extraction efficiency, analytical coverage, repeatability, and pre-analytical robustness. Coverage is assessed by the total number of detected features and the number of metabolites annotated at MSI level 1, while repeatability is determined by the coefficient of variation (CV) of variables measured across multiple parallel replicates of the same sample for each device.
This study is conducted within the framework of the PEPR SAMS MicroBe project, which relies on home-based phenotyping of 800 individuals. By supporting the technological development required for this large-scale study, this work will help identify the most suitable blood microsampling strategies for metabolomics and lipidomics applications in population-based research.

Poster P 56

Détection par spectrométrie de masse UHRMS de l'exposome médicamenteux et mise en évidence de perturbations métaboliques majeures dans une cohorte

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La santé des individus peut être évaluée de manière non invasive par l'analyse de biofluides tels que la salive ou l'urine, afin de détecter des biomarqueurs prédictifs de certaines maladies. Le métabolisme " normal " est affecté par les médicaments utilisés pour assurer un objectif thérapeutique recherché, mais aussi au travers d'effets indirects via la détoxication desdits médicaments, l'organisme maintenant une homéostasie métabolique nécessaire.

Cette étude est basée sur l'analyse des données issues de la cohorte Européenne NESCaV (Nutrition, Environnement et Santé Cardio-Vasculaire) créée pour évaluer des sujets face au risque cardiovasculaire dans des régions minières côtoyant la Wallonie. Le bras wallon (n = 504 sujets) a été phénotypé par spectrométrie de masse à résonance cyclotronique des ions à transformée de Fourier (FTICR-MS) à partir des urines prélevées chez des individus adultes. L'objectif est ici double : i) détecter la présence de médicaments prescrits, et ii) lier statistiquement la prise d'antidiabétiques avec des modifications du métabolome endogène chez les sujets concernés, en comparaison des témoins.

Grâce à une approche d'extraction des données de FTICR-MS sur R, 176000 masses distinctes ont été extraites de 650 analyses FTICR-MS à partir des données originelles. L'exposome médicamenteux est renseigné d'après les modifications moléculaires des médicaments prescrits. L'approche statistique multivariée permet aussi de détecter les métabolites endogènes d'intérêt différents de l'exposome médicamenteux. La confirmation structurale des biomarqueurs atteint un niveau élevé d'identification structurale grâce au pouvoir de résolution de la FTICR-MS, en particulier la structure fine des isotopes.

Poster P 57

MultiPlexChrom: A multiplexed approach to expand metabolome coverage and explore phytochemical diversity

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A major challenge in plant metabolomics is expanding the coverage of the metabolome and lipidome to characterize complex mixtures. Integrating complementary LC-MS approaches is one way to achieve such objective. In this study, we present a multiplexed approach to explore the chemical profile of two Artemisia species widely studied for their pharmacological properties. Dried leaf samples were extracted using a biphasic solvent mixture to capture a broad polarity range of metabolites. Extracts were analyzed by means of three orthogonal chromatographic methods, i.e., reverse-phase chromatography (C18 and lipidomic) and hydrophilic interaction chromatography (HILIC), each coupled with high-resolution tandem mass spectrometry (HRMS/MS). Building on the MS-NET workflow (Multi-Similarity Network-based annotation), which combines mass spectral similarity networks, molecular structure similarity (Tanimoto coefficient) and taxonomic information, the annotations derived from the three chromatographic methods were merged to generate a comprehensive mapping of the two species' chemical space. This multiplexed approach enabled the detection of 1979 features, 1705 of which could be annotated, offering valuable insights into the key chemical classes that differentiate between the two species. In addition, we found 94 % of the annotated features to be exclusive to one of the three chromatographic methods. Together, these findings highlight the importance of integrating complementary approaches into untargeted metabolomic workflows to navigate the chemical complexity inherent to biological matrices. MultiPlexChrom offers such a possibility and, to our knowledge, represents one of the earliest efforts in this direction.

Poster P 58

APPIN: An open-source R/Shiny tool for Automated Peak Picking and Integration of 2D NMR spectra

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1D ^{1}H NMR is widely used in metabolomics due to its speed and well-established protocols, but overlapping signals complicate signal integration, quantification and annotation. Fast 2D NMR reduces this overlap while remaining compatible with the high-throughput demand of metabolomics. However, its large-scale application remains hindered by the lack of generally accessible tools for automatically processing 2D spectra across large sample series. To address these limitations, we developed APPIN, an open-source R/Shiny application supporting various homonuclear and heteronuclear 2D NMR experiments, designed to automate processing from peak detection to integration.
The most important feature of this tool lies in intelligent multiplet handling through Density-Based Spatial Clustering. While existing tools often treat signals individually, APPIN groups correlated peaks into coherent multiplet structures, preserving structural information while simplifying integration.

The application is optimized for large-scale batch processing. Where other tools struggle with memory-intensive spectra (TOCSY file exceeds 500 MB), APPIN efficiently handles batches of more than 20 TOCSY or more than 50 COSY or HSQC spectra in a single run.

Peak detection uses two approaches: Local Maximum algorithm with clustering, or Convolutional Neural Network method trained on synthetic and experimental spectra. The interactive interface supports manual editing through box drawing, drag-and-drop refinement, and peak fusion tools. Various integration methods are available (sum, Gaussian, Voigt fitting).
The workflow is straightforward: optimize parameters on a QC sample, detect peaks, define reference areas, propagate across the batch. Validation on several datasets showed that this automated processing achieves accuracy comparable to manual analysis, while reducing processing time.

Poster P 59

Characterization of the stress-induced metabolome, proteome and physiological plasticity in different *Camelina sativa* seed tissues

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Specialized metabolites (SMs) strongly influence seed quality by modulating protein availability and stress tolerance. In *Camelina sativa*, seeds contain a diverse array of SMs whose composition is highly responsive to environmental conditions. Beyond their nutritional and antinutritional roles, SMs such as flavonoids and glucosinolates contribute to protection against desiccation, heat, and pathogens. However, the impact of environmental conditions on seed protein and mucilage composition remains poorly understood. In this study, we investigated the effects of abiotic stresses and nutrient availability on seed SM composition, protein content, and tissue-specific responses in three *C. sativa* accessions (Céline, CAM203, and CAM124). Plants were grown under control conditions or subjected to drought, high temperature, and contrasting nitrogen (N) and sulfur (S) regimes. Physiological traits were assessed at both whole-seed and tissue levels to identify genotype-specific stress responses. Whole seed and tissues physiological traits (e.g. germination performance) were measured to determine which genotypes were most impacted by each stress and which stress had the strongest impact across genotypes. Seed proteome and metabolome were analyzed using mass spectrometry across distinct seed tissues (mucilage, seed coat/endosperm, and embryo). Stress effects were strongly genotype-dependent. Nevertheless, all abiotic stresses consistently triggered substantial metabolic reprogramming in seeds. These findings reveal a conserved metabolic response to stress alongside genotype-specific regulatory patterns, providing new insights into the mechanisms underlying seed quality and stress resilience.

Poster P 60

Effet de l'élicitation par le chitosane et la mélatonine sur le métabolome de *Salvia officinalis* : approche intégrée par RMN et LC-MS

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Les plantes médicinales constituent une source majeure de produits naturels bioactifs, dont la valeur repose largement sur la diversité du métabolisme spécialisé. Dans ce cadre, les cultures in vitro représentent une plateforme pertinente pour étudier, dans des conditions contrôlées, les réponses métaboliques des plantes et orienter la production de composés d'intérêt. Parmi les approches de stimulation, l'élicitation apparaaıt comme une stratégie prometteuse pour activer ou moduler certaines voies biosynthétiques impliquées dans l'accumulation de métabolites bioactifs. Ainsi, la présente étude a évalué l'effet du chitosane (CHT) et de la mélatonine (MEL) sur des cultures in vitro de *Salvia officinalis*. Les traitements ont significativement influencé la croissance, l'initiation du cal, ses caractéristiques morphologiques, l'accumulation de biomasse ainsi que la teneur en composés phénoliques. En parallèle, l'activité des enzymes antioxydantes, notamment la superoxyde dismutase (SOD) et la peroxydase (POD), a été analysée conjointement à la capacité antioxydante mesurée par les tests DPPH et TAC. Les extraits ont également présenté des activités inhibitrices intéressantes vis-à-vis de la tyrosinase et de l'élastase, indiquant une amélioration de leurs propriétés fonctionnelles sous l'effet des éliciteurs. Afin de relier ces réponses biologiques et biochimiques aux modifications chimiques induites, les échantillons ont ensuite été analysés par résonance magnétique nucléaire (RMN) et chromatographie liquide couplée à la spectrométrie de masse (LC-MS). Le profilage métabolique a révélé une vaste diversité de métabolites ainsi qu'une différenciation nette des signatures chimiques selon la nature et la concentration des traitements. Dans l'ensemble, ces résultats montrent que le CHT et la MEL sont des éliciteurs efficaces, capables de stimuler la biosynthèse de composés bioactifs et de renforcer le potentiel biotechnologique de *S. officinalis*.

Poster P 61

Metabolomics data as ground truth for evolutionary studies

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Inference of trait evolution relies on ground-truth data. Traits are observed and measured, and their presence or absence is then used to model when they appeared. In metabolism, such traits include metabolites, enzymatic activities, and pathways. However, obtaining such observations is far more laborious than for macroscopic phenotypes. Metabolites are typically documented through natural product studies that isolate a given compound, enzymes through in vitro assays, and pathways through a combination of genomic, enzyme characterization, and metabolite isolation.

As a result, ground-truth data remain sparse across taxa because they require extensive experimental work and validation. In addition, absence is particularly difficult to establish: is a metabolite truly absent from an organism, or has it simply never been purified or detected? Because unknown states strongly reduce the power of evolutionary inference, researchers often avoid the most conservative model strategies.

In our work on benzoisoquinoline alkaloids, we observed a strong discrepancy between metabolomics data and the isolated molecules reported in the literature, including Wikidata mining. This suggests that metabolomics can fill a major gap by identifying metabolite-level trait endpoints in a rapid and scalable manner. In this communication, we argue that metabolomics has the potential to reshape studies of metabolic evolution by increasing both the coverage and the speed at which ground-truth data can be established. We support this claim with the example of benzoisoquinoline alkaloids, which we detected in at least 10 additional plant orders that are ignored in current evolutionary models, using metabolomics followed by experimental validation.

Poster P 62

Identification de nouveaux métabolites en utilisant une approche de type SQUAD MS/MS

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L'identification des métabolites en métabolomique LC-MS s'est considérablement améliorée grâce aux progrès des outils bio-informatiques. Cependant, les annotations obtenues sont au mieux de niveau 2, et le plus souvent de niveau 3. Par ailleurs, ce grand nombre de variables annotables nécessite l'utilisation de méthodes rapides (DDA, DIA), au détriment de la qualité des spectres MS/MS. De nouvelles approches MS/MS ont émergé, comme la déconvolution des spectres par la mobilité ionique, ou le SQUAD qui permet de paralléliser une détection rapide de qualité des composés connus, et l'identification de métabolites mal connus.

L'approche SQUAD a été appliquée en métabolomique non ciblée sur un spectromètre Tribrid IQ-X. Les métabolites disposant de spectres MS/MS de référence ont été validés dans la trappe d'ions, tandis que les autres variables discriminantes ont été investiguées par HCD HRMS/MS. Le temps gagné grâce à la parallélisation a permis de cibler les analyses MS/MS pour améliorer la qualité des spectres.

Les lactoyles d'acides aminés constituent un exemple d'identification de nouveaux métabolites par cette approche. En parallèle des métabolites connus, certaines variables de composés inconnus ont présenté une fragmentation de type lactoyle d'acides aminés, alors qu'aucun spectre expérimental n'était disponible en ligne. Un des protocoles de synthèse décrits dans la littérature a permis d'obtenir des standards validés par RMN. Ce protocole a d'abord été appliqué à plusieurs acides aminés apolaires, permettant la validation de leurs annotations LC-HRMS/MS. D'autres synthèses sont en cours pour obtenir des lactoyles d'acides aminés polaires, afin de pouvoir identifier l'ensemble de ces métabolites en métabolomique.

Poster P 63

Metabolomic aging clock monitors risks of cardiometabolic diseases

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Biological age clocks capture aging-related epigenetic and phenotypic alterations at molecular resolution. In particular, metabolomic clocks built with circulating compounds tracking chronological age in large-scale cohorts are hypothesised to complement epigenetic clocks and capture latent dimensions of biological aging. Leveraging 1,458 metabolites detected by untargeted UHPLC-HRMS in the Canadian Longitudinal Study on Aging (CLSA, n=9,345), we built metabolomic aging clocks in 1,100 metabolically healthy individuals and scored the metabolomic age of 8,245 metabolically unhealthy individuals. We benchmarked penalised LASSO, Elastic Net and XGBoost models to evaluate prediction robustness and structural complexity. Linear and Cox regression were fitted to evaluate chronological age- and sex-adjusted association of metabolomic clocks with CMD prevalence and incidence. The metabolomic clocks developed with several algorithms typically involve 199-208 metabolites, explaining 40%-60% of age-related variance. We further confirmed the correlation between chronological, epigenetic and metabolomic age, and their derived age gaps. Particularly, metabolomic age was validated against gold standard epigenetics (Horvath clock, based on 353 CpG sites). This metabolomic clock suggested that participants with dysmetabolism were biologically older (+5.62 years) than metabolically health individuals. Such accelerated metabolomic aging was associated with baseline inflammation (CRP, TNF-a and IL-6), insulin resistance, dyslipidaemia, and hypertension. It also predicted follow-up events of CVD, T2D, COPD, highlighting the metabolomic clock's potential for predicting adverse metabolic and cardiorespiratory outcomes which are not captured by chronological age or epigenetics. Collectively, our work reveals that metabolomic aging associates with dysmetabolism and monitors longitudinal CMD risks, where microbiome-derived metabolites play a crucial role.

Poster P 64

Assessment of multi-techniques approaches and data fusion contribution to chemical forensic: application on ricin samples

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Ricin, a toxin extracted from the seeds of Ricinus communis, is an extremely dangerous substance that can cause death at low doses. Although it is regulated by chemical and biological weapons prohibition conventions, its malicious potential is concerning due to its wide natural availability and high toxicity, as demonstrated by several historical cases.
Elucidation of the route sourcing of a ricin sample is a complex task in which chemical forensic approaches can bring relevant information. One of the major questions that can be asked to the analytical chemist is to evaluate the purification level of an unknown sample.

This preliminary study, based on a metabolomic approach, involves the analysis of crude and purified samples from several Ricinus Communis cultivars with two analytical techniques, namely 1D-1H NMR and LC-HRMS. Methods for both techniques are optimized in order to establish a small molecule profile of the different ricin samples.

Raw data are then preprocessed using open-source tools (NMRProcFlow and MZmine). Appropriate normalization and scaling methods are applied to correct dilution effects and reduce statistical bias. Data matrices are then analyzed separately using both supervised and unsupervised multivariate methods to determine discriminating variables between crude and purified samples. Last, those variables are annotated and correlations between results obtained with both analytical techniques are drawn.
Finally, the potential contribution of different data fusion strategies to chemical forensic is assessed. ComDim, a multi-block multivariate methods is assessed to analyze chemical forensic data from both analytical techniques simultaneously.

Poster P 65

Biosynthetic pathway elucidation of two C-glycosyl flavones specifically accumulated in winter flax (Linum usitatissimum L.)

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Linum usitatissimum L. (flax) is cultivated for its fibers or for its seeds rich in omega-3 fatty acids. In France, fiber yields have recently declined due to drought during the early stages of spring flax development. With climate change expected to increase the frequency of such drought events, developing winter varieties that avoid these stress periods has become a priority. However, breeding efforts are limited by insufficient knowledge of flax cold tolerance mechanisms. By using a comprehensive profiling approach, two methylated C - glycosyl flavones were recently found to accumulate specifically in winter flax varieties and were therefore proposed as potential biomarkers of cold tolerance. Using a QTL analysis to identify gene involved in their synthesis, a type I O-methyltransferase gene, *LusOMT1*, was identified as a promising candidate. In vitro assays with recombinant proteins showed that LusOMT1 specifically methylates the C -glycosyl flavones at the 7-hydroxyl position, to produce the methylated compounds. Metabolomic and gene expression analyses demonstrated a strong correlation between *LusOMT1* expression and the accumulation of these compounds in leaves and stems of both winter and spring cultivars. Furthermore, transient overexpression of *LusOMT1* in spring cultivars induced the production of the methylated molecules. To assess the physiological role of these molecules in relation to cold stress, experiments are underway to suppress their synthesis in winter varieties or introduce it into spring varieties. These findings may support the development of improved winter flax varieties and help mitigate the impact of climate change on flax fiber production.

Poster P 66

Comparison of processing tools for metabolomics by NMR

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Biofluids are challenging matrices containing hundreds of metabolites at concentrations ranging from µM to mM in water. NMR spectroscopy is a convenient analytical method to analyse such samples, and stands out for its high reproducibility, non-destructive nature, non-specificity, robustness and quantification.

While data-acquisition presents a certain level of protocol standardisation, notably with the wide use of 1H 1D experiment including solvent suppression, data-processing still lacks standardised procedures, with laboratories developing in-house software and protocols.

In this work, we attempt a holistic comparison of various available processing software. The evaluation focuses on accuracy, precision, processing time, user-friendliness and cost. Furthermore, we investigate how each software addresses common challenges in metabolomics, such as overlapping signals and low concentrations metabolites, and assess their suitability for the specific demands of metabolomics studies.

Poster P 67

Contrasting effects of seasonality and agricultural practices on periphytic biofilm metabolism and functions

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Intensive agriculture exerts strong pressure on biodiversity and the environment. Agroecological farming, promoting ecological processes and ecosystem services, appears a promising alternative to conciliate commodity production with a low environmental footprint. However, quantitative assessments of farming impacts on adjacent natural ecosystems remain limited. Aquatic environments are particularly sensitive to land-use change, making it essential to evaluate how agricultural practices influence their ecological integrity. Periphytic biofilms, complex microbial communities on submerged substrates, are relevant indicators of structural and functional biodiversity. Their rapid response to environmental variation makes them suitable for assessing agricultural effects. We investigated periphytic biofilms from two rivers, Barbanne and Engranne, along a gradient of agricultural practices (conventional, intermediate, organic). Biofilms colonized artificial substrates for four weeks during spring (May–June 2025) and autumn (October–November 2025). Functional traits (algal composition, organic matter, photosynthetic and enzymatic activities), physicochemical parameters, and microbial activity via untargeted metabolomics were analyzed. In spring, functional traits showed clear spatial separation between rivers: Engranne had more cyanobacteria and diatoms with greater organic matter, while Barbanne was dominated by green algae and showed higher copper tolerance. Multivariate analyses revealed strong seasonal structuring, distinguishing rivers and seasons but showing no clear effect of agricultural practices. Metametabolomic profiles showed the same pattern, grouping samples by season rather than farming type. Overall, seasonality explained observed variability more than agricultural practices. This study underscores the need for multi-scale, long-term monitoring to reliably evaluate agricultural impacts on aquatic ecosystems.

Poster P 68

Identification de biomarqueurs d'exposition à des mélanges complexes de pesticides chez l'huitre creuse du Pacifique (Magallana gigas) par LC-HRMS/MS

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La contamination par les pesticides est un problème très répandu dans les milieux aquatiques notamment les zones marines côtières. C'est le cas de la baie de Bourgneuf, qui abrite le plus important centre d'ostréiculture de la région Pays de la Loire et accueille également de nombreuses activités (polyculture, élevage et maraîchage) qui dépendent toutes de l'utilisation de produits phytosanitaires. L'exposition à des mélanges complexes de pesticides a déjà été signalée, chez plusieurs espèces aquatiques y compris l'hûıtre creuse du Pacifique (Magallana gigas), comme pouvant entrainer des dommages embryotoxiques, immunotoxiques, reprotoxiques, génotoxiques, et épigénétiques, ce qui menacent le recrutement, la résilience des populations et la durabilité de la production de coquillages. Cependant, les conséquences physiologiques sublétales de l'exposition aux pesticides restent mal caractérisées et il manque des biomarqueurs sensibles permettant une détection précoce.

Au cours de ce projet, des hûıtres ont été exposées (ou non) à deux concentrations d'un mélange réaliste de pesticides. Après 72 jours d'exposition, les glandes digestives ont été analysées par LC-HRMS/MS afin d'identifier des signatures moléculaires induites par l'exposition aux pesticides (biomarqueurs) et investiguer comment des mélanges complexes perturbent les voies biochimiques clés.

La validité de ces biomarqueurs candidats sera ensuite évaluée in situ chez des hûıtres transplantées pendant 12 mois sur le site de La Coupelasse (baie de Bourgneuf), afin de vérifier si les résultats obtenus en laboratoire sont transposables à des conditions environnementales pertinentes.

Poster P 69

Exploring apple specialized metabolites across the DREAM agroecosystem in the Mediterranean basin

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In the context of climate change, fruit production in the Mediterranean basin faces increasing pressures. Modern orchards are generally highly intensive systems, relying on considerable chemical inputs and low plant diversity, resulting in reduced natural habitats and loss of biodiversity. There is therefore a growing need to introduce alternative approaches that improve the resilience of fruit farms to climate change related risks, while maintaining their economic, environmental and social sustainability.

The DREAM (Diversified Orchards for REsilient and sustAinable Mediterranean farming systems) project (PRIMA, EU) promotes an agroecological approach by offering fruit growers an alternative and innovative cultivation system that supports high-quality and diversified fruit production. This system integrates the selection of fruit varieties, improvement of the ecosystem using cover crops, agroforestry and adoption of regulated deficit irrigation strategies.

As a part of this project, we investigated the specialized metabolome of apple fruits cultivated in Italy under both conventional and DREAM agroecosystems. Specialized metabolites (SMs), including polyphenols and vitamins, are key contributors to fruit quality and are known for their beneficial effects on human health. In addition, they contribute to fruit defence against pests and abiotic stresses. Using an untargeted metabolomic approach based on LC-MS/MS, we characterized and compared the SMs profiles in both the peel and flesh of apple fruits across the two cultivation systems. This work will contribute to a better understanding of how innovative agroecosystems can influence fruit metabolite composition, and therefore support the development of more sustainable and resilient fruit production systems in the Mediterranean basin.

Poster P 70

Dynamic In Situ Characterisation of Grapevine Volatiles via Drone-Mounted Sampling and GC-MS Analysis: Advancing Chemical Ecology in Viticulture

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Volatile organic compounds (VOCs) emitted by plants mediate critical biotic and abiotic interactions, including defence mechanisms and interplant signalling. However, the interpretation of volatilome remains a challenge due to the chemical complexity and multidimensionality of the interaction network involved. Actual sampling methods are often limited by experimental bias such as the enclosing in chambers that modify the interactions with the environment.

The INRAE Explor'AE DRONESRENIFLEURS project addresses this limitation through a miniaturised, 3D-printed sampling device, controlled by Arduino board and deployed via drone. This system enables non-invasive and spatial evaluation of VOC emitted by grapevine at different phenological stages. VOC are adsorbed on stir-bar sorptive extraction (SBSE), then desorbed thermally to mass spectrometry gas chromatography (GC-MS) analysis. Preliminary trials, conducted at controlled air volumes (10 cm3 to 2000 cm3), are ongoing to determine optimal sampling time and volumes, while validating the device's sensitivity and efficiency.

This project has methodological challenges linked to field conditions, especially wind influence, atmospheric pollution and VOC competition on SBSE surface. Nevertheless, it will open perspectives to better understand volatilome dynamics in real conditions and ultimately contribute to new protection strategies based on chemical ecology.

Poster P 71

NMR metabolic profiling of midgut Babesia bovis-infected ticks to improve control strategies for cattle vector-borne diseases

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Vector-borne diseases (VBDs) are caused by pathogens transmitted by vectors, such as mosquitoes or ticks and are spread worldwide.1 Recent studies have highlighted the relationship between vector microbiota composition and VBDs, by either enhancing or preventing pathogen transmission.2,3 Studies in ticks have already highlighted the metabolic changes induced by microbiota perturbation, which influence tick physiology and vector viability. For instance, NMR-based metabolomics has contributed to the identification of metabolic-mediated pathways for tick immunity activated with antimicrobiota vaccines, which increase resistance to pathogen colonization, in particular for Borrelia, which cause Lyme borreliosis.4

Babesia bovis is one of the causes of Babesiosis in tropical and subtropical regions. This VBD is transmitted by the tick Rhipicephalus microplus. It is economically the most important and necessary to mitigate because all the livestock loses that it generates worldwide. It has been demonstrated that Babesia infection causes modifications in the microbiota of the cattle tick R. microplus.6 The metabolic changes still need to be confirmed and described. Here, both infected and non-infected controls were collected from cattle after 15 days of feeding. Ticks were dissected either the same day of the collection or 72h after the collection (incubation at 28°C and 80% humidity).7 Polar and non-polar metabolites were simultaneously extracted from ticks' midguts using a modified Folch's method.8 NMR metabolomics multiparametric approaches have led to the profiling and identification of potential biomarkers for each infection status and time point.

1) https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases
2) https://doi.org/10.1007/s00203-021-02506-0
3) https://doi.org/10.1038/s41564-022-01099-8
4) https://doi.org/10.1093/femsec/fiaf082
5) https://doi.org/10.1021/acs.analchem.6b04420
6) https://doi.org/10.3389/fmicb.2025.1608409
7) http://doi.org/10.1016/j.vetpar.2015.06.016
8) https://doi.org/10.1038/nprot.2007.376

Poster P 72

Metabolomic Insights into Tomato Root Responses to Meloidogyne incognita Infection and α-Aminobutyric Acid Treatment

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Southern root-knot nematode (Meloidogyne incognita) is a major soil-borne pathogen responsible for significant yield losses in crops worldwide. Infection induces metabolic reprogramming in plant roots, which can be exploited by the nematode to support its parasitism. Aminobutyric acid isomers are non-proteinogenic amino acids known to enhance plant tolerance to abiotic and biotic stresses, however, their physiological impact and mechanisms of action remain poorly understood. The objective of this study is to investigate the metabolomic changes associated with nematode infection and to characterize the biochemical responses of tomato Moneymaker following aminobutyric acid treatment.
An untargeted metabolomics approach was performed using four-dimensional trapped ion mobility spectrometry (4D-TIMS) on tomato's roots subjected to nematode inoculation and α-aminobutyric acid (AABA) treatment. First, we demonstrated a clear metabolic dysregulation in tomato roots following nematode infection. Discriminating metabolites were mainly associated with amine-derived hormone metabolism and the biosynthesis of secondary metabolites.

We then assessed the metabolic changes induced by AABA treatment in both control and inoculated tomato roots. AABA treatment markedly altered the metabolic profile of control roots, with 318 and 231 features differentially expressed in positive and negative modes, respectively, compared to untreated controls. Notably, AABA treatment led to a significant upregulation of the GABA biosynthetic pathway in tomato roots.
Overall, this study highlights the potential of untargeted metabolomics to deepen our understanding of plant–pathogen interactions and the mechanisms underlying tomato resistance induced by AABA treatment. These findings open new perspectives for identifying metabolic targets to modulate nematode behavior and improve plant protection strategies

Poster P 73

Développement et harmonisation d'un workflow de métabolomique spatiale (MALDI-qTOF)

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Au cours de la dernière décennie, l'imagerie par spectrométrie de masse (MSI) s'est imposée comme une technique incontournable pour l'analyse spatiale des métabolites et lipides dans les tissus biologiques. Son développement répond à une demande croissante d'information biochimique spatialement dans les domaines suivants : la découverte de biomarqueurs, la médecine personnalisée, la métabolomique (1)... Cependant, malgré son potentiel analytique majeur, les workflows MSI souffrent actuellement d'un défaut d'harmonisation (2).
Dans le cadre de ce projet, nous proposons une étude intra-laboratoire pour la standardisation de l'approche métabolomique par MALDI-MSI. Nos travaux concernent :

- La comparaison des modalités de calibration : calibration interne/externe (MALDI ou ESI, avec ou sans lock mass) ;
- Les méthodes de normalisation appliquées à diverses droites de quantification (TIC, RMS et Based-peak) ;
- La mesure de la variabilité intra-laboratoire sur une série de foie de souris (n=5).

En perspective de cette étude, nous prévoyons de partager nos résultats et méthodes avec des membres du GDR-MSI pour réaliser une étude inter-laboratoire.

Cette démarche vise à établir des recommandations préliminaires sur les bonnes pratiques méthodologiques en MSI, en mettant l'accent sur la robustesse métrologique des images générées. Par la suite, les résultats de cette étape de pré-validation seront présentés à la communauté du GDR-MSI afin de favoriser le partage de méthodes harmonisées et d'initier une réflexion collective sur les standards qualité en MSI.

(1) Swales et al., " Mass spectrometry imaging and its application in pharmaceutical research and development ".
(2) Barry et al., " Multicenter Validation Study of Quantitative Imaging Mass Spectrometry ".

Poster P 74

Independent cohort integration of the blood metabolome and lipidome reveals systemic energy metabolic and hemorheological adaptations to hypoxia in humans in the highest city of the world (5100m)

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Chronic hypoxia associated with high-altitude residence represents a major environmental constraint requiring profound biological adaptation. While adaptive mechanisms allow many highlanders to maintain physiological homeostasis, prolonged exposure can lead to maladaptive conditions such as chronic mountain sickness (CMS). This study aimed to characterize metabolic and erythrocyte adaptations to chronic hypoxia.

We integrated untargeted blood (plasma and erythrocytes) metabolomic and lipidomic data from two independent human cohorts within the Expedition 5300 research program, including individuals living at distinct altitudes. Multivariate hierarchical models, redundancy analyses, and machine-learning approaches were applied to jointly analyse datasets.

The plasma metabolome robustly discriminates the living altitude and reveals a remodelling of energy metabolism. Metabolites related to fatty acid B-oxidation are reduced with decreased oxygen availability ($p < 0.01$). Concomitantly, increased circulating Nicotinamide and Lactate levels confirm the shift toward anaerobic glycolytic metabolism. CMS severity is specifically associated with reduced Nicotinamide levels among individuals living at very high altitudes, revealing a potential target to limit CMS. At the erythrocyte level, we identified distinct lipid clusters, associated with blood viscosity, erythrocyte deformability and aggregation, and haemoglobin concentration. Notably, a specific phosphatidylserine species -PS(16:0/18:1)- is associated with increased haemoglobin concentration ($p < 0.01$), potentially suggesting impaired eryptosis. Our results reveal adaptations to chronic hypoxia involving modulation of energy metabolism and erythrocyte membrane composition. Nicotinamide availability and specific erythrocyte lipid signatures emerge as key determinants of successful adaptation or maladaptation to high altitude.

Poster P 75

RDynLib 2.0: High-Throughput LC-MS Metabolomics Data Archiving and Analysis

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We present RDynLib 2.0, an R package for LC-MS-based high-throughput, experiment-wide metabolomics data archiving and analysis. RDynLib 2.0 is a newly developed addition to the RforMassSpectrometry ecosystem and seamlessly integrates with existing infrastructure for LC-MS experiments and mass spectral analysis, including xcms, MSnbase, Spectra, MsExperiment, and CompoundDb.

RDynLib 2.0 enables experiment-wide selection and archiving of representative fragmentation spectra for all detected features, alongside MS1 spectra, feature intensities, and experimental metadata. Experiments acquired on distinct MS instrument types, such as QTOF instruments and ion trap instruments, are archived in specific DynLib subdatabases and aligned so that multiple complementary spectra can be retrieved for the same compound. RDynLib 2.0 also provides functions to aid the structural elucidation of unknowns through Candidate Substrate-Product Pair (CSPP) networks, GNPS-like networks, and integrated spectral analysis. The power of combining these complementary data is illustrated by the characterization of a novel class of highly conjugated metabolites in flax seed integuments. Constructing an in-house DynLib database with RDynLib 2.0 enables cumulative knowledge building by archiving data from multiple past metabolomics experiments. Our DynLib database contains complementary spectra for over 20,000 identified or partially characterized compounds from more than 30 plant species, including QTOF MS/MS and multilevel ion trap MS spectra in positive and negative ionization modes, together with annotated MS1 spectra and experiment-level metabolite relationships. This resource is particularly well suited to support future AI-based approaches, enabling the development of information-rich embeddings optimized for plant metabolites and the characterization of previously unknown compounds.

Poster P 76

Characterization of metabolic interactions and metabolisms within the cyanosphere

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Cyanobacteria are autotrophic bacteria playing a key role in aquatic ecosystem function by producing O and organic compounds through photosynthesis. Nevertheless, they represent also a threat for health due to increasing blooms that can be highly toxic because of toxins production by certain cyanobacteria. If abiotic factors such as temperature, nutrients are contributors to these harmful events, several studies have highlighted the importance of the cyanobacterial microbiome in bloom formation and persistence. Indeed, cyanobacteria are often associated with various heterotrophic bacteria such as Roseomonas, Blastomonas, and Rhodobacter, which interact continuously with their host and may influence their metabolism. To unlock these interactions, untargeted metabolomics is a powerful approach due to its sensitivity and its ability to detect a wide range of metabolites, including unknown compounds, providing a comprehensive overview of metabolic exchanges. In this context, the present study aims to understand how heterotrophic bacteria may contribute to bloom formation through metabolic interactions within the cyanosphere by using an untargeted UPLC-HRMS/MS metabolomics approach. To do so, following 14 days cultivation of axenic cyanobacteria / bacteria and xenic cultures under various temperature and nutrient conditions, endo and exometabolic samples were investigated at various time through multiplexing mono and biphasic extraction methods and chromatographic separation. Data were processed using MZmine for matrix generation, MetaboAnalyst and R for statistical analysis. Features were annotated through a combination of SIRIUS and MSNet, further allowing the establishment of structural similarity networks. Data analysis is still ongoing while preliminary chemometrics (PCA, HCA) highlighted discrepancies between the tested conditions.

Poster P 77

Evaluation of a New Chemical Label BASA: A Comparison with Gold Standards

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Personalized medicine involves tailoring medical treatments to the unique characteristics of each individual. However, significant challenges remain in understanding the molecular mechanisms underlying many diseases. Metabolomics, the study of small molecules within biological systems, holds great promise for advancing personalized medicine through molecular level insights. By combining derivatization and LC-MS, it is possible to achieve metabolite identification, enhancing both the sensitivity and coverage of analyses. In our study, we introduce BASA as a derivatization reagent. After identifying the specific fragmentation patterns of BASA-derivatized compounds, a library of approximately one hundred molecules was derivatized to compare BASA with four commercial chemical labels. In addition to its versatility, BASA allowed for sample analysis in negative mode, further increasing analytical sensitivity. Negative mode presents an opportunity for untargeted analysis of biological samples due to reduced background noise. Combined with specific fragments, BASA-derived compounds seem promising for metabolomic exploration. Further studies are needed to fully demonstrate their contributions to exploring complex biological environments.

Poster P 78

Rôle des polyamines dans la virulence de Pseudomonas aeruginosa au cours de l'infection pulmonaire chronique chez les patients atteints de mucoviscidose

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Les polyamines (polyA) sont des composés organiques impliqués dans plusieurs processus cellulaires. Notre groupe a montré, par analyses métabolomiques comparatives non ciblées de souches de *Pseudomonas aeruginosa* (Pa) issues des voies respiratoires de patients CF, une corrélation entre une production accrue de polyA et une altération de la fonction pulmonaire.

Cette étude multi-omique vise à comprendre comment Pa module sa production de polyA chez les patients CF, son effet sur l'expression des facteurs de virulence et si Pa contrôle ses phases de virulence en modulant la production de polyA lors d'infections chroniques.

Des analyses génomiques et transcriptomiques ont servi à élucider les mécanismes de modulation des polyA. Des mutants isogéniques de Pa bloquant partiellement ou totalement les voies de production de polyA ont été générés. Des expériences ont permis de mesurer la virulence de souches mutantes produisant des niveaux de polyA, évalués par LC/HRMS.

Les résultats ont identifié 38 gènes surexprimés dans les isolats à forte production de polyA, dont des gènes du système de sécrétion de type 3 (T3SS) et de motilité. Parmi eux, *speE2* et *speD2* semblaient responsables de l'augmentation de la spermidine, soulignant le rôle des voies alternatives dans la production de polyA. Les polyamines synthétisées par la voie alternative contribuent davantage à la cytotoxicité que celles produites par la voie classique.

En conclusion, cette étude démontre le rôle crucial des voies biosynthétiques alternatives des polyA dans la virulence de Pa et suggère de nouvelles cibles thérapeutiques contre les infections chroniques chez les patients CF.

Poster P 79

Automated mapping of metabolomic compounds onto metabolic networks using MetaNetMap

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Understanding biological systems requires integrative and multi-level approaches. Genome Scale Metabolic Networks (GSMNs), that are derived from genome annotation, capture the metabolic capabilities of an organism. In contrast, metabolomics gives an insight into what is really happening in an organism under specific conditions. Mapping molecules identified from metabolomic experiments onto GSMNs offers several advantages: mapped compounds can be used for visualisation or quality assessment of the GSMN; and conversly, unidentified metabolites highlight gaps in the network and create model curation opportunities. This is especially important for specialised metabolism that is currently largely overlooked in GSMNs. Such mapping is thus attractive but it remains cumbersome due to several challenges such as harmonisation and matching of identifiers between metabolomic annotation profiles and GSMNs, and dispersion of information across various knowledge bases and input files. Currently, mapping requires manual or semi-manual mapping, but it is quite fastidious and prone to errors.

To overcome these challenges, we developed MetaNetMap, a Python package that automatically matches metabolite information between metabolomic annotations and GSMNs. It improves mapping rates through direct mapping taking into account metadata of input files, indirect matching by relying on conversion data tables built from third-party knowledge bases, and partial matching techniques. It offers an automatic solution for ambiguous mapping, providing relevant information for manual curation.

By automating and harmonising metabolite mapping, MetaNetMap aims to overcome a major barrier in multi-omic integration, enabling more efficient and reproducible integration of metabolomic data onto GSMNs.

Poster P 80

Iron Competition As The Mediator In Probiotic Inhibition Of Chytridiomycosis In The Era Of The Holobiont

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Widespread declines in amphibian populations have been linked to a fatal skin disease, chytridiomycosis. The infection, largely caused by one strain of fungus, Batrachochytrium dendrobatidis, affects the host's ability to control homeostasis, leading to cardiac arrest due to an electrolyte imbalance. With the explosion of the global pet trade and an ever-changing climate, global populations are under enormous stress while mitigating strategies remain expensive and in their infancy. As complex biological systems move out of obscurity, an amphibian's holobiont becomes an invaluable resource to probe for disease resistance. Our study targets nutrient competition as a mechanism of inhibition against B. denrobatidis. Limitation of Iron has been employed by bacteria, plants and host immune systems to effectively inhibit fungal growth. Siderophores are high-affinity iron-chelating compounds, used to outcompete for iron uptake. Here, we targeted iron competition as a mechanism for disease resistance. Bacteria isolated from frogs' dermal tissues were grown in iron depleted media, stimulating the production of siderophores. Using untargeted native LC-MS methods we systematically identified both known and unknown siderophores. A siderophore database was then built using MzVault for real time library searches and future dereplication. Diluted supernatants enriched with bacterial siderophores exhibited inhibition of chytrid growth.

Poster P 81

Multiblock integration of LC–HRMS (ESI+/ESI-) and NMR data enhances marker discovery and composition analysis of turmeric food supplements

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Turmeric-based dietary supplements (TFS) are widely consumed for their presumed health benefits, but their chemical composition varies greatly depending on the formulation. In a previous study, we showed substantial variability among nineteen TFS using an untargeted metabolomics approach based on liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) in both positive and negative ionization modes. Although complementary, these two modes had been analyzed separately.

In the present study, we adopted a multiblock integration strategy to jointly analyze LC-HRMS data (positive and negative modes) together with nuclear magnetic resonance (NMR) data. This approach aimed to leverage the complementarity of these analytical platforms to obtain a more comprehensive characterization of turmeric-based supplements and to identify the key metabolites responsible for the observed variability. The identification of these markers was further strengthened through the use of variable-selection models. The data were processed using four multiblock methods: Block-PLS-DA (with variable selection based on VIP scores or correlation circles), DIABLO, and asmbPLS-DA (with variable selection in an automatic mode).

The results showed that all four models improved the assessment of compositional variability, enabling better separation of TFS and clearer discrimination between different formulations. They also revealed the metabolites contributing most to these differences through variable selection. These models displayed distinct specificities, making them complementary tools for data exploration and interpretation.

Poster P 82

High-throughput LC–MS metabolomics workflow integrating automated sample preparation for high-coverage metabolomic profiling of human serum: Application to a Clinical Cohort

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Metabolomics provides a systems-level view of biological processes, complementing genomics, transcriptomics, and proteomics, and supporting clinical applications. Automated sample preparation is critical to improve throughput, reproducibility, and standardization in large-scale studies. We developed a high-throughput untargeted LC–MS workflow integrating automated robotic sample preparation with mass spectrometry analysis. This workflow was applied to 818 human serum samples from the Descendance clinical cohort to generate a robust metabolite dataset for future clinical integration. Samples were processed using a Janus G3 (Revvity) liquid handling system with methanol quenching and protein precipitation, followed by vacuum drying and reconstitution prior to LC–MS analysis. Data were acquired in positive and negative ionization modes using an Orbitrap Exploris™ 240 mass spectrometer. After preprocessing, quality filtering (reproducibility and linearity criteria), and batch correction, 818 annotated metabolites were retained across diverse chemical classes. Metabolite origin classification was performed using MetOrigin 2.0, integrating KEGG, HMDB, DrugBank, ChEBI, FooDB, T3DB, and BiGG databases. The dataset included metabolites of host (204), microbiome (309), dietary (581), and xenobiotic origin. Notably, a single metabolite may belong to multiple categories. Quality control assessment demonstrated < 30% inter-batch relative standard deviation (RSD) for all annotated metabolites in pooled QC samples and < 5% intra-batch RSD for internal standards. This large-scale untargeted metabolomics workflow demonstrates strong analytical robustness and broad serum metabolome coverage. The resulting dataset constitutes a valuable resource for integrative analyses linking metabolic profiles to clinical and epidemiological data.

Poster P 83

Improving the robustness of an internal UPLC-DAD-HRMS/MS databasis by implementing retention indices for reliable metabolite identification in metabolomics datasets

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The cosmetics and beauty industry thrives on consumer preferences, with a growing emphasis on natural ingredients that are safe for consumers and beneficial for the environment, being non-ecotoxic and sustainably sourced.

In this context, natural cosmetic ingredients are developed from various natural sources which need a deep understanding of their chemical composition to ensure safety and quality. We commonly use untargeted liquid chromatography - mass spectrometry (LC-MS) based metabolomics to explore and characterize the chemistry of our raw material with the request of various libraries. Despite advances in high-resolution mass spectrometry, the lack of retention time reproducibility across different laboratories and instruments hampers the use of shared libraries for Level 1 identification ((i)). In this study, we propose a transition from absolute retention time to Linear Retention Indices (LRI) using a homologous series of twenty N-alkylpyridinium-3-sulfonates (NAPS-RM-RILC, RI 100-2000) as a scale.

We first conducted a comprehensive robustness study, comparing LRI and Rt stability across multiple variables: LC systems, column aging/batches, temperature, and inter-day/inter-operator variability. The LRI approach demonstrated significantly lower deviations, confirming its reliability for inter-platform data alignment. Based on these findings, we developed an in-house database containing LRI data for 1200 authentic standards. This workflow successfully bridges the gap between untargeted screening and definitive identification, providing a scalable and transferable solution for the high-throughput characterization of complex natural extracts.

(i) Schymanski E. L. et al.; Identifying Small Molecules via High Resolution Mass Spectrometry: Communicating Confidence; Environ. Sci. Technol., (2014); 48: 2097–2098.

Poster P 84

D4P (Dereplication4Plants)

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Les approches non ciblées de métabolomique par chromatographie liquide couplée à la spectrométrie de masse haute résolution (LC-HRMS) se sont fortement développées chez les plantes. Elles représentent aujourd'hui un levier stratégique pour identifier des biomarqueurs moléculaires impliqués dans l'acclimatation aux stress abiotiques et biotiques. La caractérisation structurale de ces composés et l'identification des réseaux de gènes associés ouvrent la voie à des approches d'écologie chimique visant à mieux gérer les cultures et à renforcer leur résistance aux ravageurs.
L'annotation des profils métabolomiques reste un défi majeur, en raison de la diversité des métabolites, du manque de structuration des connaissances et de la forte dépendance à une expertise manuelle en chimie analytique. Malgré les progrès des outils de similarité spectrale, la rigueur nécessaire à l'interprétation limite encore la reproductibilité et la réutilisation des données.

Pour surmonter ces contraintes, un système d'information structuré, centré sur une base de déréplication, est en cours de développement à l'IGEPP à partir des données issues de la plateforme P2M2. Ce dispositif, nommé D4P, intègre en continue des annotations détaillées de molécules d'intérêt agroécologique.
Basé sur le web sémantique, D4P assure une diffusion normalisée des données et s'appuie sur des ontologies de référence (ChEBI, PubChem, NCBI...) pour garantir interopérabilité et pérennité. En combinant structuration sémantique et formats spectrométriques standards (MGF, MSP), D4P vise à devenir une ressource de référence pour la déréplication des métabolites végétaux, favorisant la fiabilité et le partage des annotations LC-HRMS au service de la recherche en écologie chimique et génétique environnementale.

Poster P 85

Métabotype des patients atteints d'hypertension pulmonaire associée aux maladies pulmonaires interstitielles

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Contexte
L'hypertension pulmonaire associée aux pneumopathies interstitielles diffuses (ILD-PH) est une affection sévère, sans traitement spécifique efficace. Sa forte hétérogénéité clinique suggère une variabilité biologique importante et la nécessité d'un meilleur phénotypage. Hypothèse Nous avons émis l'hypothèse que le métabotype sérique de patients permettrait d'identifier des signatures associées à l'ILD-PH et de caractériser des biomarqueurs de sévérité et de traits cliniques pertinents.

Méthodes
Des échantillons sériques des cohortes françaises HYPID et HYPID-2 ont été analysés par spectrométrie RMN IVDR (Bruker B.I. Methods 2.0, 600 MHz iVDR ; B.I.Quant-PSTM 2.0), identifiant 41 métabolites et 114 paramètres lipoprotéiques. Ces valeurs absolues ont été comparées aux intervalles de référence pour chaque patient, puis intégrées aux variables cliniques et hémodynamiques. Des analyses univariées non paramétriques (Wilcoxon-Mann Whitney, Kruskall-Wallis) et multivariées (PCA, WGCNA) ont été réalisées.

Résultats
165 échantillons appariés ont été analysés. Plusieurs métabolites présentaient des écarts aux valeurs de référence : acides aminés (phénylalanine +46%, glutamate +53%), métabolisme énergétique (lactate +21%, pyruvate +257%) et lipoprotéines faibles. Le profil global apparaissait homogène en PCA, suggérant une signature systémique commune. PCA et WGCNA montrent une corrélation entre sévérité de l'ILD-PH et un module enrichi en acides organiques et corps cétoniques (Pearson r=0,23, p=0,008).

Conclusion
Le métabotype issu de patients des cohortes HYPID/HYPID-2 révèle des perturbations systémiques mesurables par rapport aux normes cliniques dans l'ILD-PH. Cette approche non destructive et fondée sur des concentrations absolues sériques, permet un phénotypage biologique et constitue un outil pertinent de stratification des patients.

Poster P 86

La métabolomique par ^{1}H-RMN révèle une différence dans les profils métaboliques des patients intoxiqués au protoxyde d'azote et ceux présentant un déficit en vitamines B9 et B12

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L'usage récréatif du protoxyde d'azote (N2O) provoque l'inactivation des vitamines B9 et B12, induisant une inactivation fonctionnelle des voies métaboliques liée à ces vitamines. Le but de cette étude vise à comparer les profils métaboliques des consommateurs avec des patients présentant des déficits en vitamine B9 et B12.
154 échantillons de plasma hépariné ont été collectés au sein du service des urgences du CHU de Lille. Ils ont été répartis en 3 groupes : Consommateurs de N2O (N=79), non-consommateurs carencés en vitamines B9 et B12 (N=32), et non-consommateurs non-carencés (N=43) (définis selon les valeurs de références du laboratoire). Les échantillons ont ensuite été analysés par RMN en vue d'obtenir des profils métabolomiques non ciblés. Après bucketing, les données ont été analysées par diverses approches, dont la PLS-DA.

Les analyses ont permis de discriminer les différents groupes. Premièrement, une séparation significative (R2=0,567 et Q2=0,341) peut être observée entre les consommateurs et les non-consommateurs. Deuxièmement, lorsque l'on s'intéresse uniquement au déficit en vitamines B9 et B12, une différence significative (R2=0,622 et Q2=0,392) peut être observée entre les consommateurs de N2O et les patients carencés.
Bien que préliminaires, ces résultats illustrent qu'il existe des différences dans le profil métabolomique entre les consommateurs et les non-consommateurs de N2O. Ces résultats semblent également montrer que les perturbations biologiques d'un patient N2O diffèrent de la seule carence en vitamine B12, ouvrant la voie à des investigations plus globales pouvant expliquer la physiopathologie, et de possibles nouveaux traitements différents de la supplémentation vitaminique seule.

Poster P 87

Approches métabolomiques ciblées par UHPLC-MS pour l'étude de la stabilité dans le temps d'échantillons de vins monovariétaux

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Les approches métabolomiques sont particulièrement adaptées à l'étude de sujets complexes tels que la traçabilité du vin, le développement de nouveaux cépages résistants ou les relations entre la composition et les caractéristiques de qualité du vin. Cependant, cette matrice étant en constante évolution, l'une des principales préoccupations consiste à déterminer comment conserver les échantillons avant leur analyse (1). Cette question revêt une importance particulière lors d'études métabolomiques collaboratives mobilisant différentes plateformes.

Depuis deux ans, nous analysons les effets du stockage d'échantillons de vin à différentes températures. Nous avons sélectionné 38 vins français monovariétaux, commerciaux, provenant du Pays d'Oc. Les échantillons de vin ont été stockés dans des Eppendorf à température ambiante, 4◦C, -20◦C et -80◦C. Les analyses ont été réalisées après 6 mois, 1 an, 1,5 ans et 2 ans à l'aide d'un système UHPLC-HRMS/MS. Une analyse ciblée des polyphénols a été menée à l'aide d'une courbe d'étalonnage couvrant plus de 50 polyphénols (2).

Des tests ciblés préliminaires à 2 mois ont déjà montré une différence significative entre les échantillons conservés à 4◦C et ceux conservés à température ambiante. En comparaison, l'analyse n'a montré aucune différence significative pour la plupart des polyphénols conservés à -20◦C ou -80◦C. En comparant ces échantillons à ceux conservés à 4◦C, nous avons observé une stabilité des acides phénoliques , des réponses variables chez les flavonols et les stilbènes, et une perte marquée de tous les flavanols . Des recherches supplémentaires seront menées afin d'identifier d'autres biomarqueurs spécifiquement impliqués dans ces distinctions.

Poster P 88

A robust untargeted metabolomics workflow for large human cohort studies

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Precision medicine's success depends on collecting high-throughput data from large populations, yet current untargeted metabolomics workflows face limitations in processing and annotating ultra high performance liquid chromatography-high resolution mass spectrometry (UHPLC-HRMS) data at scale(1). Here, we introduce an untargeted metabolomics workflow optimized for deep characterizations in large-scale studies involving thousands of biological samples.
Key components of this workflow to enhance annotation depth include the acquisition of study samples using data-dependent acquisition (DDA) across multiple ionization modes, the generation of additional MS/MS spectra through intelligent DDA applied to quality control samples, feature annotation via interrogation of multiple in-house and public spectral databases, and the characterization of unannotated features using in silico approaches.

Data robustness was ensured through sample randomization and automated metabolite extraction and preparation using a liquid-handling robot operating in 96-well plate batches, enabling the analysis of up to 500 samples per week. Instrument performance was online monitored using internal standards. During post-acquisition analysis, five methods for correcting intensity drift and batch effects were benchmarked, and stringent feature filtering was applied using dilution series and blanks to remove extraction artifacts and low-quality signals.

We applied this workflow to a study comprising +2000 human plasma samples, identifying over 600 distinct metabolites (excluding in silico annotations), demonstrating its applicability to human cohort studies.

Bibliography: (1) Stancliffe E et al. Anal. Chem. 2022, 94, 50, 17370–17378

Poster P 89

Approche multi-omique de l'état sanitaire de l'anguille européennes des lagunes et cours d'eau de Méditerranée occidentale

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Depuis la fin du 20 siècle, l'anguille européenne (*Anguilla anguilla*) a subi un déclin dramatique, avec une réduction de ses effectifs de plus de 90 % sur l'ensemble de son aire de répartition, principalement en raison de la rupture de la continuité écologique, de la surpêche, des contaminations chimiques et biologiques (parasites et autres pathogènes). Malgré les mesures entreprises pour permettre la préservation de cette espèce (essentiellement régulation de la pêche), sa population ne montre toujours pas de signe de rétablissement. Le projet AnguillaMed se propose donc d'évaluer l'état sanitaire des anguilles dans 11 sites méditerranéens de la zone POCTEFA (unités territoriales des Pyrénées-Orientales, de Gérone et de Barcelone) incluant des fleuves, rivières et lagunes et de faire le lien avec leurs différents niveaux de pression anthropique. Les objectifs principaux du projet sont 1) d'analyser les niveaux de contamination des anguilles par des méthodes conventionnelles nécessitant la dissection des individus (niveaux de contaminations par des polluants chimiques dans le muscle et le foie, et d'infestations par bactéries, virus et macro-parasites, transcriptome de la rate), et 2) de développer des méthodes innovantes et non létales pour leur suivi à long terme. Parmi celles-ci figure l'étude des métabolites et du microbiome associés au mucus cutané. Le poster présente la variabilité chimique du mucus cutané des anguilles collectées dans les 11 sites sélectionnés des côtes catalanes françaises et espagnoles. Il présente également les premiers résultats d'intégration des données de transcriptomique de rate et de métabolomique du mucus cutané.

Poster P 90

Identification of isoprenoid quinones in environmental lipidomes using molecular networking

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Isoprenoid quinones are lipophilic molecules found in almost all organisms and are known to shuttle electrons within electron transport chains (ETCs), playing an essential role in bioenergetic processes such as respiration and photosynthesis. Ubiquinone (UQ or coenzyme Q) and plastoquinone (PQ), for example, have been extensively studied for their involvement in mitochondrial and chloroplastic ETCs, respectively. Both are found in the microbial world, alongside a dozen other quinone types that have been discovered to date. However, several findings suggest that a wider variety of isoprenoid quinones likely exists, as evidenced by the recent discovery of methylplastoquinone (mPQ) in Nitrospirota (Elling et al., PNAS, 2025). In fact, all currently characterized microbial quinones have been described in cultivated organisms, leaving the quinone content of most uncultivable bacteria and archaea unexplored. This project aims to unveil the full extent of quinone diversity in the environment by exploring the lipidomes from complex microbial communities. A strategy built as a modular analytic pipeline, based on untargeted lipidomics, which relies on high-resolution tandem mass spectrometry (MS/MS) coupled with molecular networking tools. This approach takes advantage of the fragmentation pattern shared by all quinones to cluster them together, allowing their identification and annotation. Preliminary results provided complete quinone inventories for complex samples and uncovered novel candidates, including new chain and headgroup variants with distinct modifications. In a later phase, metagenomic–lipidomic correlations will link quinones to their producing organisms, providing new insights into our understanding of quinone evolution and distribution, shedding light on new quinone biosynthetic pathways.

Poster P 91

Proteomic signature of small extracellular vesicles reveals biomarker candidates for moderate asthma of racehorses

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Diagnostic confirmation of moderate asthma (MA) of horses currently relies on bronchoalveolar lavage fluid (BALF) cytology, Small extracellular vesicles (sEV), carrying bioactive molecules, have emerged as promising tools for biomarker discovery in respiratory diseases.
BALF from both right and left lungs was prospectively collected on 32 racehorses in active training. sEV were isolated within 12 hours, characterised (size, concentration, morphology and proteins), and their content analysed by high-resolution (MALDI-TOF) mass spectrometry for proteomic investigation. Bioinformatic analyses were first conducted on all BALF samples from MA vs. control (CTL), irrespectively to the lung side; left and right BALFs were then independently compared among and within groups. Significance criteria were Fold Change > 1.5 and $p < 0.01$, respectively.

Six horses were excluded because of other respiratory conditions; leading to 13 MA and 13 CTL horses finally included. Overall, 17 differentially expressed proteins (10 upregulated, 7 downregulated) were found in BALF of MA vs. CTL horses. Similarly, 28 proteins were up and 4 downregulated in the right BALF, and respectively 7 and 4 proteins in the left BALF. None of these significantly identified proteins were differentially expressed when comparing BALF from left vs. right lungs within either MA or CTL groups. Three proteins (Pentraxin-3, LOC100064703 and S100-A9) were consistently upregulated across MA vs. CTL comparisons. These proteins are linked to regulation of phagocytosis, neutrophil aggregation, and antimicrobial activity.
These preliminary results both suggest the involvement of sEV in the pathophysiology of MA and identify putative biomarkers for asthma of horses.

Poster P 92

1H-NMR metabolomic analysis of plasma and rumen fluid from lambs to identify metabolic markers associated with rearing practice

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Separating lambs from their mothers at birth is a common practice in dairy systems to increase milk production. However, this practice is associated with health issues, which can lead to reduced growth. The objective of this study is to identify metabolic markers of the rearing practice. Two groups of lambs were reared either with their mothers (n=5 x 2) or separated (n=5 x 2) and were sampled one week apart prior to weaning. Metabolomic fingerprints of plasma and rumen fluid were acquired on a 500 MHz NMR spectrometer using CPMG and NOESY sequences, respectively. Data processing was performed using NMR-PROCFLOW, and statistical analysis was conducted using BioStatFlow. Principal component analysis showed a clear separation of plasma depending on rearing method whereas no separation was observed in the rumen fluid profiles. The fold-changes analysis of signal intensities depending on the rearing method in plasma and rumen fluid led to 40 and 31 VIPs, respectively. Plasma of lambs separated from their mothers presented lower relative concentrations of valine, leucine, isoleucine, isobutyrate, 3-hydroxybutyrate, β-hydroxyisovalerate, and 1-methylhistidine. Rumen fluid of lambs separated from their mothers presented higher relative concentrations of glucose, and lower relative concentration of phenylacetate and isobutyrate. These results show that metabolite concentration in the plasma may be more sensitive to the rearing method compared to the rumen fluid. Further investigations are necessary to explain the differences of metabolites relative concentrations.

Poster P 93

Leveraging High-Throughput LC-MS Metabolomics to Unlock the Potential of Fruit Tree Crop Wild Relatives for Sustainable Agriculture

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Crop Wild Relatives (CWRs) are wild plant species genetically related to domesticated crops, offering a rich yet underexplored source of biochemical and genetic diversity, particularly valuable for improving the resilience, sustainability, and nutritional quality of fruit crops. While current fruit production depends on a limited pool of elite cultivars, exploring and characterizing diversity across wild and cultivated populations is essential to reintroduce beneficial traits into commercial varieties and to develop biodiversity-based crop management tools. The FruitDiv project integrates metabolomics with global multi-omics approaches, including genomics and phenomics, to investigate core collections of Malus, Pyrus, and Prunus. By profiling metabolites associated with key agronomic traits such as fruit quality, stress tolerance, and resistance to pest and disease, FruitDiv aims to elucidate genotype-to-phenotype relationships and develop pioneering technology for phenotypic trait prediction.

An untargeted LC-MS workflow was applied to over 1,500 leaf and fruit samples of Prunus. Samples underwent automated ethanolic extraction, including Quality Controls preparation, followed by UHPLC-LTQ Orbitrap analysis in negative ion mode. Data processing, annotation and statistics were performed using MS-DIAL and MetaboAnalyst. Further computational modeling is ongoing to build predictive models linking biomarkers of plant performance and fruit quality. Preliminary results indicated clear metabolomic shifts between cultivated and CWRs of apricot, highlighting key redox and secondary pathways involved, consistent with genomic studies (Groppi et al., 2021). Beyond advancing scientific knowledge on fruit crop adaptation, highthroughput metabolomics also provides key insights into the potential of CWRs to address challenges related to climate change, sustainable agriculture, and global food security.

Poster P 94

Functional responses of river benthic microbial communities to environmental fluctuations associated with global change

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Benthic microbial communities are complex assemblages constituting a fundamental compartment of aquatic ecosystems, playing a key role in ecological processes such as primary production, organic matter recycling, and biogeochemical nutrient fluxes. In the current context of climate change, these communities face rising water temperatures and growing fluctuations in discharge, which may result in repeated drying events of variable duration affecting stream width. Although the effects of temperature elevation or hydrological drying have been relatively well studied, the effects of larger environmental fluctuations associated with climate change remain poorly understood. Yet, their amplification is likely to induce shifts in both the structure (taxonomic composition and diversity) and functioning (physiological processes) of microbial communities. In this context, the ReFFE project aims to determine the extent to which, and through which mechanisms, the hydro-thermal history of benthic microbial communities in rivers may affect their structure, functioning, and stability when facing additional stressors. To address this objective, several laboratory experiments were conducted to assess the effects of water level variations and thermal fluctuations on the structure, functions, as well as the resistance and resilience of benthic microbial communities to short-term additional stressors. Analysis of the meta-metabolome of these communities will provide deeper insight into how microbial communities adapt to hydrological and thermal fluctuations at the molecular and biochemical levels, and will help establish the link between community functions and resistance to additional stressors.

Poster P 95

STERONLINE project : Development of an adapted steroidomics analytical strategy to improve the knowledge of endometriosis physiopathology and boost the identification of diagnostic biomarkers

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Endometriosis is a systemic, steroid-dependent, inflammatory disease characterized by the growth of endometrial-like tissue outside the uterus, affecting approximately 10 % of women of childbearing age. The etiology and pathophysiology of endometriosis is not completely understood to support effective treatment and prevention strategies. Despite the steroid dependency, little is known concerning the underlying metabolism of estrogen and other tightly related steroids. Moreover, shortening the long diagnostic delays is a major priority in endometriosis research.
In this context, the main aim of the project will be to develop a global steroidomics analytical strategy to improve the knowledge of endometriosis pathophysiology and boost the identification of diagnostic biomarkers.

Currently, we offers a methodology targeting thirty steroids in various human matrices. This methodology requires several steps of sample preparation to enable a sensitive quantification of steroids, but all theses steps are expensive and time-consuming. A new method aiming at providing a faster and cost effective monitoring of a large panel of steroids is currently under development. The method allows the detection of molecules belonging to the corticoid, androgen, estrogen and progestagen groups in serum and urine by HPLC-HRMS with online SPE system.
The new analytical strategy will be applied on urine and blood from a clinical study consisting of 135 patients with and without endometriosis. Samples will be analyzed both using the targeted steroid approach developed, as well as a more global approach aimed at broadening the scope of investigation beyond these compounds in order to explore all metabolites accessible to analysis.

Poster P 96

Apple fruit as a rapid model to assess Neofusicoccum parvum virulence and phytotoxin production

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Neofusicoccum parvum is a widespread fungal pathogen capable of infecting numerous plant species, including major fruit crops such as apple, peach, and grapevine. These infections cause significant economic losses worldwide, particularly under changing environmental conditions that can weaken plant defenses. Previous studies have shown that differences in pathogenicity among N. parvum strains are associated with variations in phytotoxin production.

In this study, we developed a rapid and efficient infection model using apple (*Malus domestica*) fruit to assess fungal virulence and associated metabolic changes. By combining targeted and untargeted metabolomic approaches, we monitored disease progression and toxin accumulation. Within less than two weeks, infected apples exhibited intense browning followed by tissue decay, with symptom severity depending on the fungal strain. Highly aggressive strains induced pronounced necrosis that strongly correlated with elevated levels of the polyketide (-)-terremutin.

Untargeted metabolomic profiling revealed distinct molecular signatures between strains, with numerous polyketides enriched in apples infected by the most aggressive isolate. Targeted analyses further demonstrated that (-)-terremutin accumulated as early as three days post-inoculation, reaching peak levels at nine days, while remaining significantly lower in infections caused by less aggressive strains. Multivariate discriminant analysis identified both shared and strain-specific metabolites among the top features with the highest Variable Importance in Projection (VIP) scores.

Overall, this work establishes apple fruit as a simple and reliable model for rapidly evaluating *N. parvum* virulence and phytotoxin production, and highlights phytotoxins as early biomarkers for pathogen detection in plant tissues.

Poster P 97

Assessment of the fate and impacts of a bioherbicide in soil through the integration of untargeted metabolomic and metabarcoding approaches

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Biopesticides are complex products derived from natural sources such as plants and microorganisms, and they represent promising alternatives to synthetic pesticides. However, current pesticide regulations are not fully adapted to these biobased products, and their effects on living organisms remain insufficiently characterized.
In this study, a 57-day microcosm kinetics experiment was carried out, during which soil samples were collected at six time points (T000, T002, T008, T014, T028, and T057). Untargeted metabolomic analyses (LC-HRMS) and molecular profiling (16S and 18S rRNA gene metabarcoding) were combined to investigate the fate of the natural extract biopesticide Beloukha and its impacts on soil microorganisms.

Concerning its environmental fate, the results indicate that resilience was not achieved within 57 days after Beloukha application. Modeling approaches estimated that complete dissipation would occur approximately 125 days after treatment. With regard to biological impacts, bacterial communities were affected at T000, T002, and T014, while microeukaryotic communities showed changes at T000, T002, and T028. No significant impact was detected on metazoan communities. Correlation analyses between metabolomic data and microeukaryotes suggested that Beloukha compounds especially polyethylene glycols (PEGs) influenced several bacterial and microeukaryotic genera.
Overall, the findings suggest that Beloukha and its degradation products exert a limited impact on prokaryotic and microeukaryotic species. These advances, based on high-throughput approaches, contribute to the development of methodologies for identifying chemical and biological pollution markers associated with biopesticide application. It is an essential step for regulatory purposes, as conventional pesticide assessment frameworks are not fully suited to complex natural substances.

Poster P 98

Impact de solutions microbiennes sur la réponse métabolique du chien lors d'une transition brutale vers un régime hyperprotéiné : une approche multi-niveau

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L'introduction brutale d'un régime hyperprotéiné chez le chien peut perturber l'homéostasie digestive et métabolique. Cette étude visait à caractériser, à l'aide d'un cadre méthodologique intégratif, la reconfiguration hôte–microbiote induite par un stress nutritionnel aigu et à comparer les effets de deux solutions microbiennes distinctes : un probiotique (Saccharomyces boulardii, SB) et un postbiotique (Lactobacillus helveticus, HA122).
Après 30 jours d'une diète de référence, de SB ou de HA122, les chiens ont subi un passage direct vers une diète hyperprotéinée, tout en maintenant la supplémentation. Des prélèvements fécaux et sanguins ont été réalisés à J30 et J36. Analyses suivantes ont été faites : le microbiote intestinal par séquençage 16S rRNA, la métabolomique et l'évaluation de la fonction muqueuse intestinale (IgA, calprotectine, α1-antitrypsine). Les données ont été structurées en blocs fonctionnels (microbiote, métabolome, biochimie) et intégrées via des analyses multivariées (WGCNA, PLS-DA), puis organisées en graphes de connaissances spécifiques à chaque condition.

Chez les chiens recevant placebo, le changement alimentaire a induit une reconfiguration coordonnée impliquant le catabolisme des acides aminés, le métabolisme des purines et nucléotides et la fonction muqueuse intestinale. Les deux solutions microbiennes ont modulé ces reconfigurations selon des signatures distinctes : SB a été associé à des modules liés à la signalisation cellulaire et au turnover nucléotidique, tandis que HA122 a structuré des réseaux liés au métabolisme énergétique, à l'équilibre redox et à des régulations épigénétiques.
Cette étude multi-blocs illustre l'intérêt des approches systémiques multi-blocs pour discriminer des modes d'adaptation métabolique distincts lors d'un stress nutritionnel aigu.

Poster P 99

Chilling injury to algal symbionts induces host starvation and metabolic reorganization in a temperate cnidarian

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Global temperature anomalies increasingly disrupt the cnidarian-algal symbiosis through a phenomenon termed bleaching. In contrast to heat stress, the mechanisms underlying symbiotic breakdown under cold stress remain largely unknown. Combining physiological and metabolomic measurements, we investigated the response of the photosymbiotic sea anemone holobiont Aiptasia couchii to an experiment mimicking a cold spell in the Mediterranean Sea. Within four weeks, we observed the onset of symbiotic breakdown reflected in reduced algal endosymbiont density and chlorophyll a content. While photosynthetic efficiency remained largely unaffected, no gross photosynthesis was detectable in cold-stressed anemones and decreases in glycosyldiacylglycerols and fatty acyl glycosides indicated chloroplast lipid remobilization. This breakdown of symbiotic carbon cycling was reflected in increased dipeptide and ceramide levels suggesting anemones catabolized protein reserves and induced pre-apoptotic pathways. Taken together, these responses suggest a decoupling of light and dark reactions of photosynthesis in cold-stressed endosymbionts, resembling chilling injury in higher plants and free-living microalgae. This chilling-induced collapse of symbiotic nutrient cycling eventually leads to host starvation in cold-stressed Cnidaria. Hence, while cold and heat stress may invoke contrasting physiological effects on endosymbionts, our results suggest that both stressors destabilize the symbiosis through similar mechanisms rooted in host starvation.

Poster P 100

Integrative NMR and LC-MS metabolomics approach to assess the effects of biotic and abiotic contaminants on European Eel

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In their natural environments, aquatic animals are exposed to a wide range of environmental stressors, typically classified as biotic or abiotic. Within the INTERACTION project, the biotic stressor under investigation is the parasitic nematode *Anguillicola crassus*, which is known to significantly impair eel migration[1], while the abiotic stressor is Bisphenol S, an emerging contaminant of increasing concern due to its potential effects on aquatic organisms2. To assess the metabolic impacts of these stressors under controlled experimental conditions, metabolomics approaches are employed alongside other omics tools. A non-invasive method based on skin mucus analysis has been developed, and a multiblock strategy integrating NMR and LC-MS metabolomics has been implemented for whole-body analysis in eels.

Here, we present preliminary results obtained from samples specifically designed for the optimization of analytical methods. Several metabolite extraction procedures were evaluated (100% Methanol, methanol/water 70:30, and methanol/water 50:50) in order to improve extraction robustness and reproducibility. Comparative analyses indicated that the 100% methanol protocol provided the most reproducible metabolic profiles for eel tissues, and was therefore selected as the reference extraction procedure for subsequent NMR metabolomics analyses. In parallel, optimization of extraction conditions for LC-MS analyses is still ongoing. These methodological optimizations are essential to ensure robust and reliable comparison of NMR metabolic profiles between experimental conditions (healthy vs. *Anguillicola crassus*-infected eels), and represent a critical step toward consistent integration of NMR and LC-MS datasets within the multiblock framework.

1. Bourillon B., Sci Total Environ, 2020, 743: 140675.
2. Shanika, Sci Rep. 2025, 15, 9560.

Poster P 101

Breast cancer metabolism and responsiveness to dichloroacetate: relationships with 15N and 13C natural abundance

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Background: Metabolic reprogramming is a hallmark of breast cancer (BrCa). While isotope tracing is well-established, natural isotope abundance is emerging as a novel biomarker for metabolic alterations. We investigated how cancer-associated reprogramming and Dichloroacetate (DCA) treatment, a pyruvate dehydrogenase kinase inhibitor, influence these isotopic signatures.

Methods: Two BALB/c mammary tumor models (V14 and 4T1) were used to assess the relationship between isotopic composition and metabolism. We integrated isotopomics, metabolomics, and lipidomics data to characterize the effects of DCA on tumor growth and metabolic flux.

Results: Both tumor models exhibited significant enrichment and depletion compared to healthy tissue. Multivariate analysis identified isotopic features as key discriminators between malignant and normal tissues. Notably, V14 and 4T1 displayed distinct nitrogen metabolism: V14 tumors were more depleted and showed higher sensitivity to DCA. DCA treatment modulated values in a tumor-specific manner, increasing them in V14 while decreasing them in 4T1, reflecting shifts in the arginine-to-ornithine ratio and nitrogenous metabolite pools. In contrast, values remained stable under DCA, primarily driven by the balance between lipid and TCA cycle intermediates rather than glycolytic flux. Changes in lipidomics, specifically shorter fatty acid tails in phosphatidylcholines, further supported the isotopic shifts observed in V14 tumors.

Conclusions: These findings demonstrate that BrCa metabolic reprogramming directly influences natural isotope abundance. The correlation between shifts and lipid-derived nitrogen signatures highlights the potential of natural abundance isotopomics as a promising tool for non-invasive metabolic profiling and monitoring treatment response.

Poster P 102

Untargeted MS-based lipidomics methodology for studying changes in Arabidopsis thaliana lipid droplets during heat stress and recovery

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Liquid chromatography coupled with high-resolution mass spectrometry is a leading technique to study metabolism. Here, we present an untargeted lipidomics approach based on chromatographic separation using a less nonpolar stationary phase in reverse LC "Phenyl-Hexyl" coupled with Q-TOF data-dependent mass spectrometry acquisition. This allows separation of lipid species across various classes, including neutral lipids (monoacylglycerols, diacylglycerols, triacylglycerols), phospholipids, galactolipids, ceramides, alkyl cinnamates, free fatty acids, and sterol-class lipids.

Our main approach to lipid annotation is based on spectral comparison via propagation of annotations from molecular networks, using class-specific fragments (https://lipidomicstandards.org/lipid- class-specific-fragments), as well as in silico search tools like SIRIUS and machine learning tools such as ms2query. This enabled building a spectral and RT m/z database containing 1,030 and 500 features in electrospray positive/negative, respectively. We applied this approach to investigate heat stress effects and the role of LDAP1 protein in lipid droplets of Arabidopsis thaliana during stress and recovery.

Lipid droplets are storage organelles with distinct protein composition and dynamics in vegetative tissues and seeds. In vegetative tissues, they are scarce, transient, and coated with Lipid Droplet Associated Proteins. To address this, we analysed lipid remodelling during HS (3 h at 37°C) and recovery (24 h at 22°C) in two-week-old A. thaliana seedlings. Our strategy produced robust and comprehensive lipid profiles (1659 features, QC CV < 25%, 240 unique lipid species). Results reveal lipid species with specific dynamics during HS and/or recovery. Some lipids show altered dynamics in the ldpa1 mutant compared to wild type, including TAGs containing polyunsaturated fatty acids.

Poster P 103

Annotation of the Biotransformed Metabolome Using Untargeted Metabolomics UHPLC-HRMS and Pseudo-MS^3/MS^3 Strategies

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The gut microbiota influences human pathophysiology through host-microbial metabolic interactions. Several cardiometabolic diseases are linked to conjugated microbial metabolites including steatotic liver disease and diabetes. However, systematically annotating these conjugated metabolites remains a major challenge in metabolomics, as they are not widely described in databases, and reference standards are limited and costly.
In this study, we developed an analytical workflow combining ultra-high-performance liquid chromatography and high-resolution mass spectrometry (UHPLC-HRMS) with neutral loss (NL) screening and guided pseudo-MS^3/MS^3 approaches for structural identification. Human serum samples were analyzed using a Vanquish Duo Orbitrap Exploris™ 240 with optimized in-source fragmentation (0-50 V) and an Orbitrap IQ-X Tribrid system in both positive and negative ESI modes. Chromatographic separation was achieved on a Hypersil GOLD™ C18 column using a rapid methanol gradient. Data processing was performed in R to screen 41 predefined modification types, followed by manual validation and confirmation using chemical standards.

A total of 11,928 features were detected with the Exploris 240 system, including 462 annotated metabolites after reproducibility filtering (RSD< 30%), with 165 at MSI level 1 and 297 at MSI level 2. NL screening revealed numerous signatures, enabling the identification of 42 previously unannotated sulfated and glucuronidated metabolites using GNPS and mzCloud libraries. Optimal in-source fragmentation was achieved at 30 V.

Applied to the Descendance cohort (n = 818), this workflow detected over 6,000 NL-associated features in plasma. This approach improves the detection of conjugated metabolites, expanding metabolome coverage and providing new insights into host-microbiota interactions and the dark metabolome.

Poster P 104

Rôle des perturbateurs endocriniens dans le déclin des populations d'amphibiens – analyse métabolomique intégrée par RMN du proton et LC-HRMS

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Des études récentes suggèrent que les effets métaboliques transgénérationnels induits par les perturbateurs endocriniens (PE) sont des facteurs impliqués dans le déclin des populations d'amphibiens.
Nous souhaitons comprendre comment les PE obésogènes agissent chez les amphibiens. Pour répondre à cette question, nous avons étudié les effets d'un mélange de 6 PE à des doses environnementales sur 3 générations de *X. tropicalis* (F0 exposée, F1 et F2 non exposées). Afin de comprendre la contribution précise de chaque sexe dans la transmission des désordres métaboliques, plusieurs modalités d'accouplement ont été réalisées (mères et pères non exposés ; mères exposées avec pères non exposés ; mères non exposées avec pères exposés ; et mères et pères exposés). Les perturbations métaboliques ont été évaluées pour chaque génération par une approche métabolomique par RMN du proton et chromatographie liquide couplée à la spectrométrie de masse haute résolution (LC-HRMS) au niveau hépatique et des œufs, chez des mâles et des femelles.

Les analyses statistiques multivariées par bloc ou multi-blocs appliquées aux données RMN et LC-HRMS de la génération F0 n'ont pas permis de mettre en évidence des signatures métaboliques différentes entre les animaux témoins et les animaux traités. La méthode Consensus OPLS-DA a permis de montrer des différences entre les animaux de la génération F1 dont les 2 parents ont été exposés et les animaux dont les deux parents n'ont pas été exposés pour le foie chez les mâles et les femelles et les œufs.
Ces premiers résultats montrent les potentialités de la métabolomique intégrée en toxicologie environnementale.

Poster P 105

Metabolome-metagenome network analysis in cardiometabolic diseases

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Cardiometabolic diseases, including type 2 diabetes and ischemic heart disease (IHD), are characterized by chronic low-grade inflammation, gut microbiome dysbiosis, and persistent alterations in circulating metabolites. Resolving host-microbiome molecular interactions remains costly and challenging. To address this, we developed a bioinformatic tool to 1) construct multi-organism metabolic networks linking enzymes and metabolites across multiple species, 2) navigate this network via topological analysis and 3) visualize shortest paths and key nodes in the network. We hypothesized that this network-based approach could help elucidate the bidirectional communication between the host and the microbiome.

We applied this workflow to the MetaCardis study1 (n = 1,241), including healthy individuals (n = 275) and patients with IHD (n = 372) with matching metagenomics and metabolomics. We built a network incorporating 31 IHD-enriched microbial species and 224 IHD-associated serum metabolites and then performed topological analysis. Gene-metabolite pairs derived from IHD-enriched microbial taxa and IHD-associated metabolites exhibited significantly shorter path distances than unrelated pairs under a random model ($p = 0.004$), indicating a structured association between microbial enzymes and metabolites altered in IHD. Topological analysis identified high interconnectivity among indole-derived conjugates, branched-chain amino acids, and succinate. Enrichment analysis revealed enhanced D-amino acid turnover and secondary bile acid remodeling in IHD patients ($p < 1 \times 10$).

These results indicate that network-based multi-omics integration provides a systems-level approach to uncover host-microbiome molecular interactions underpinning cardiometabolic disease physiology.

Poster P 106

A combined experimental and computational strategy for the analysis of ultra-short peptides (USPs)

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The analysis of ultra-short peptides (USPs) remains challenging due to the large number of possible molecules (168,400 di-, tri-, and tetrapeptides), the high occurrence of isobaric species, and the limited structural information available from mass spectrometry. As a result, USPs remain poorly characterized in protein hydrolysates.
This work aims to develop a robust strategy for USP peptidomic analysis, initially focusing on dipeptides as a model system.

A combined computational and experimental approach was implemented. A dataset of 400 dipeptides was characterized using 211 molecular descriptors, followed by statistical analysis to explore the physicochemical space. This enabled the selection of 41 representative dipeptides, covering the diversity of the dataset, which were subsequently synthesized. Chromatographic separation was optimized, and mass spectrometry data were investigated to assess their analytical potential.

The proposed approach highlights the critical role of chromatographic orthogonality. Only 14 out of 41 dipeptides were adequately resolved under reversed-phase conditions, while these same peptides were better separated using HILIC. These results demonstrate the necessity of combining complementary separation methods to achieve reliable peptide discrimination prior to mass spectrometry analysis.
Overall, this work demonstrates that integrating multiple separation strategies and incorporating retention time information are essential for effective USP characterization. This study lays the foundation for a robust analytical pipeline dedicated to the analysis of USPs in protein hydrolysates from the agri-food industry, with the aim of improving their valorisation.

Poster P 107

Positionnement de doubles liaisons sur des N-acylhomosérine lactones par une réaction de dérivatisation photochimique de Paternò-Büchi

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Les N-acylhomosérine lactones (AHLs) représentent une classe de molécules de signalisation chez les bactéries, jouant un rôle dans le mécanisme de communication bactérien appelé Quorum sensing (1). Ces molécules sont caractérisées par une structure bipartite : une tête homosérine lactone lié à une chaine acyl. La diversité structurale des AHLs réside dans la longueur de la chaine acylée, le degré d'insaturation et la présence ou l'absence d'un hydroxyle ou d'une cétone en position 3 de la chaine carbonée (2). Ces différences influencent les spécificités de réponses cellulaires des différentes souches et sont par conséquent importantes à caractériser. Pour leur caractérisation structurale, la MS/MS par CID ne permet pas de positionner les doubles liaisons (3). Cette contrainte peut être surmontée par une dérivatisation par la réaction photochimique de Paternò-Büchi. Un réactif cétonique, sous exposition à la lumière UV réagit avec la double liaison de l'AHL, résultant en la formation d'un cycle oxétane. Des expériences en MS/MS par CID permettent la détection de fragments caractéristiques et ainsi de positionner la double liaison. Cette méthode peut être implémentée en solution ou en ligne entre le système chromatographique et le spectromètre de masse. La mise en œuvre de cette méthode et les résultats obtenus seront discutés.

1. A. M. Stevens et al. Chem. Rev. 2011;111:4–27.
2. M. E. A. Churchill et al. Chem. Rev. 2011;111:68–85.
3. C. Gosset-Erard et al. Anal. Bioanal. Chem. 2024;416:5431–5443.

Poster P 108

An Adjustable Workflow Integrating Experimental and Computational Approaches in Metabolomics and Lipidomics

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At the Institut Pasteur, the Metabolomics Core Facility (MCF) supports researchers in untargeted metabolomics and lipidomics studies by accompanying them from experimental design to data analysis and interpretations.
A protocol, adaptable to diverse scientific projects and ensuring results reliability and reproducibility, is fundamental.

In this poster, we present the workflow implemented on the platform and highlight its interoperability and its role as an interface between biologists and bioinformaticians.

Within the context of untargeted metabolomics and lipidomics, our platform generates high-quality LC-HRMS MS/MS data using both an Orbitrap Exploris 240 (HILIC column, negative mode) and an Orbitrap IQ X Tribrid (C18 column, positive and negative modes).

In addition to the vendors' software, bioinformatics tools, more suited to the platform's needs, are developed according to the analytical methods established by the MCF.

Post-acquisition data quality control is performed using FreeStyle 1.8 (Thermo Fisher Scientific) and LabMS (developed at MCF). The data are processed using MZmine (v. 4.8.0) (running on HPC) to generate the features table, which is then analyzed using MetaboAnalyst (v. 6.0) and an in-house RShiny application to explore the metabolic profiles.
To validate this workflow, we are collaborating with Pedro ESCOLL and Paula MARTINEZ- OCA (Institut Pasteur, Biology of Intracellular Bacteria) on the "MetaBact" project. Our experiments aim to understand the metabolic changes induced by infection intracellular bacteria Legionella pneumophila in human primary macrophages, which represent a challenge for current methods and therefore require innovative solutions such as those presented here.

Poster P 109

Investigation of baobab fruit maturity using wet-chemistry, Near-infrared, Nuclear Magnetic Resonance and Liquid Chromatography-Mass Spectrometry

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The baobab tree (*Adansonia digitata L.*) native to African continent has remarkable resilience and supports both ecosystems and human communities. Its fruit, highly valued for its dietary and therapeutic properties, has transformed from being a traditionally consumed wild fruit into a popular ingredient worldwide. Even though baobab trees are well adapted to harsh climatic conditions prevailing in African Savannah, environmental factors influence fruit development, ripening and overall quality. This study focuses on determining changes in key maturity indices and metabolite composition during ripening of baobab fruits. It also seeks to identify region specific metabolites and metabolic biomarkers signalling the right harvesting stage for baobab fruits. Baobab fruits were collected from coastal and inland Kenya during the onset of ripening and at an interval of 3.0 and 1.5 weeks for coastal and inland regions, respectively. Key maturity attributes; moisture content (MC) titratable acidity (TA), soluble solids (SS), and potential of hydrogen (pH) were determined. The TA, TSS, and pH evolved during early to mid-maturity stages followed by inconsistencies, while MC dropped consistently as ripening progressed. Portable near-infrared spectroscopy (NIRS) was also evaluated for rapid, accurate and non-invasive determination of maturity attributes. With support vector machine algorithm, NIRS could be used for rapid determination of baobab shell moisture content. To comprehensively profile metabolite composition of baobab fruit pulp, an approach combining NMR and LCMS was employed. A sample preparation protocol, compatible with both analytical techniques was developed. Profiling and monitoring of metabolites during maturation of baobab fruits are currently underway.

Poster P 110

High-Throughput Metabolomics in Freshwater Periphyton: A Pilot Study of Multi-Class Pesticide Risk Assessment

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Facing increasing chemical pollution of aquatic ecosystems, there is an emerging need to improve the risk assessment at microbiome level. However, the application of metabolomics to microbial communities (i.e., meta-metabolomics) remains limited. We previously developed a high-throughput meta-metabolomics workflow in aquatic periphyton encompassing robotic extraction, R package Dromics to evaluate aggregated meta-metabolome response and sensitivity threshold. Here, we validate this workflow by screening six pesticides with diverse modes of action: herbicide metolachlor, fungicides azoxystrobin and boscalid, insecticides fenoxycarb, imidacloprid and chlorpyrifos. Metolachlor, azoxystrobin and boscalid induced significant shift in periphyton meta-metabolome. 259 to 359 features following dose-response trends with FDR < 0.05. Interestingly, while the insecticides did not induce significant global metabolomic changes, fenoxycarb exhibited the highest number of features (n = 600) shown dose-response relationships. 68 and 19 features displayed dose-response relationships for imidacloprid and chlorpyrifos, respectively. Benchmark-doses (BMDs–1SD) were calculated from each fitted dose response model. Fenoxycarb exhibited the lowest median BMD of 6.0 × 10^{-3} mg/L, followed by azoxystrobin (1.8 × 10^{-1} mg/L), chlorpyrifos (2.8 × 10^{-1} mg/L) and imidacloprid (4.7 mg/L). Metolachlor and boscalid exhibited the highest median BMDs (16.4 mg/L). Trend analysis showed that metolachlor and boscalid primarily elicited decreasing trends, suggesting an inhibitory damage response. Conversely, fenoxycarb curves were predominantly biphasic (Uand bell-shape), indicating a defense or compensatory response to this insect growth regulator. Following feature annotation via the newly released MS-Net workflow, we will further elucidate the specific metabolic classes and potentially associated pathways impacted by these contaminants.

Poster P 111

Metabolomics analysis of human keratinocyte response to chemical sensitizers

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Allergic contact dermatitis (ACD) is a common skin disease caused by drugs and environmental chemicals acting as ”chemical sensitizers”. Keratinocytes (KCs), the main component of the epidermal barrier, play a crucial role in initiating and developing inflammatory responses by releasing proinflammatory cytokines into the skin microenvironment. In this study, we investigated the impact of three chemical sensitizers - hydroxycitronellal (HC), cinnamaldehyde (CINA) and methylisothiazolinone (MIT) - on the metabolome of human primary KCs using a metabolomics approach.
Normal human primary epidermal KCs were exposed to HC, CINA or MIT at two different concentrations for 1h, 6h, or 24h. The intracellular metabolome of sensitizer-treated cells and vehicle controls (0.1% H2O or DMSO) was analyzed using C18- and HILIC-based liquid chromatography coupled with high-resolution Q-Orbitrap mass spectrometry (LC-HRMS) (n = 12 per group). In parallel, a panel of proinflammatory cytokines was quantified in the extracellular medium (n = 3 per group).

A total of 181 endogenous metabolites were annotated with high or medium confidence levels (1 or 3 according to Sumner et al., 2007) after data processing and feature annotation using an in-house spectral database. Significant metabolic changes were observed in sensitizer-treated cells showing time-, sensitizer- and concentration-dependent variations. Although the three chemical sensitizers induced distinct modifications in the abundance of various intracellular metabolites, several key metabolic pathways were commonly affected across all treatments.
These findings provide a strong foundation for further investigations into the role of metabolic remodeling in the inflammatory response of KCs to chemical sensitizers in ACD.

Poster P 112

Remodelage des lipoprotéines HDL-ApoA1 chez les patientes atteintes d'un cancer du sein sous chimiothérapie, l'apport du métabotype par spectroscopie RMN IVR

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Contexte :

La chimiothérapie provoque un stress métabolique systémique important chez les femmes atteintes d'un cancer du sein. Les lipoprotéines HDL et leur principale protéine structurelle, l'ApoA1, participent activement au transport inverse du cholestérol et à l'homéostasie vasculaire. La spectroscopie RMN IVDR permet une analyse détaillée des profils lipoprotéiques circulants. Les lipoprotéines HDL et leur principale protéine de structure, l'ApoA1, sont centrales dans le transport inverse du cholestérol et l'homéostasie vasculaire. La spéctroscopie RMN IVDR donne la possibilité d'une caractérisation fine des profils lipoprotéiques circulants

Hypothèse :

Le métabotype, en particulier les paramètres liés aux HDL, pourrait constituer un biomarqueur de la détérioration métabolique induite par la chimiothérapie.

Méthodes :

Des échantillons sériques de la cohorte ASTER-T (232 patientes, deux prélèvements à 6 mois) ont été analysés par RMN IVDR afin de quantifier 114 paramètres lipoprotéiques. Les patientes ont été réparties en deux groupes : chimiothérapie (n=110) et témoin (n=122). Les données longitudinales ont permis d'évaluer la variabilité intra-individuelle de chaque paramètre par le coefficient de variation (ΔCV = écart-type/moyenne). Des analyses statistiques univariées et multivariées ont été réalisées.

Résultats :

À l'inclusion comme à 6 mois, les concentrations de triglycérides, cholestérol total, HDL-cholestérol et HDL-ApoA1 étaient comparables entre les groupes. En revanche, l'analyse longitudinale a montré une augmentation marquée de la variabilité intra-individuelle dans le groupe chimiothérapie, notamment pour HDA1 (11,17 % vs 3,7 %), HDCH (9,78 % vs 4,31 %) et TPTG (15,49 % vs 0,49 %).

Conclusion :

Le remodelage HDL-ApoA1 observé sans modification globale des concentrations suggère une altération dynamique du transport du cholestérol en réponse au stress métabolique induit par la chimiothérapie.

Informations pratiques

Plan d'accès

Gare Lille Flandres
Lille Flandres

Gare Lille Europe
Lille Europe

Lieu du congrès
Lille Grand Palais

Lieu des ateliers du 19 mai
Institut Gernez Rieux

Dîner de gala
Palais de la Bourse de Lille

Les deux gares de Lille (Lille Flandres et Lille Europe) se situent à quelques minutes à pied l'une de l'autre.

Le congrès du 20 au 22 mai se déroulera à Lille Grand Palais, à 9 minutes à pied de la gare Lille Flandres.

Les ateliers du 19 mai auront lieu à **l'institut Gernez Rieux (IGR) au CHU de Lille** : 2 Rue du Dr Schweitzer, 59000 Lille. Emprunter le métro ligne1 et sortir à l'arrêt CHU – Centre O. Lambret (700 m).

Merci à tous·tes pour votre participation

Un grand mèrchi à tertous d'êt v'nu et d'avou participé !