



Infrastructure for Omics Tecnologies

Genomics, Proteomics and Metabolomics for the scientific community





INFRAESTRUCTURAS CIENTÍFICAS Y TÉCNICAS SINGULARES (ICTS)



OmicsTech

Infrastructure for Omics Tecnologies

Genomics, Proteomics and Metabolomics for the scientific community

Is a distributed ICTS formed by the Centro Nacional de Análisis Genómicos (CNAG), the CRG/UPF Proteomics Unit and the Center for Omic Sciences (COS-URV/Eurecat)



Make the most out of your omics projects!

www.omicstech.com









JROPEAN UNION uropean Regional evelopment Func Ina manera de hacer Euron:

ONDO EUROPEO D DESARROLLO

UNIÓN EUROPE



INFRAESTRUCTURAS CIENTÍFICAS Y TÉCNICAS SINGULARES (ICTS)



QmicsTech



Genomics Area CNAG and COS

cnag

centre nacional d'anàlisi genòmica centro nacional de anàlisis genòmico



Proteomics Area CRG and COS

> FONDO EUROPEO DE DESARROLLO REGIONAL



Metabolomics Area COS







	GOBIERNO DE ESPAÑA	MINISTERIO DE CIENCIA E INNOVACIÓN	

i Universitats



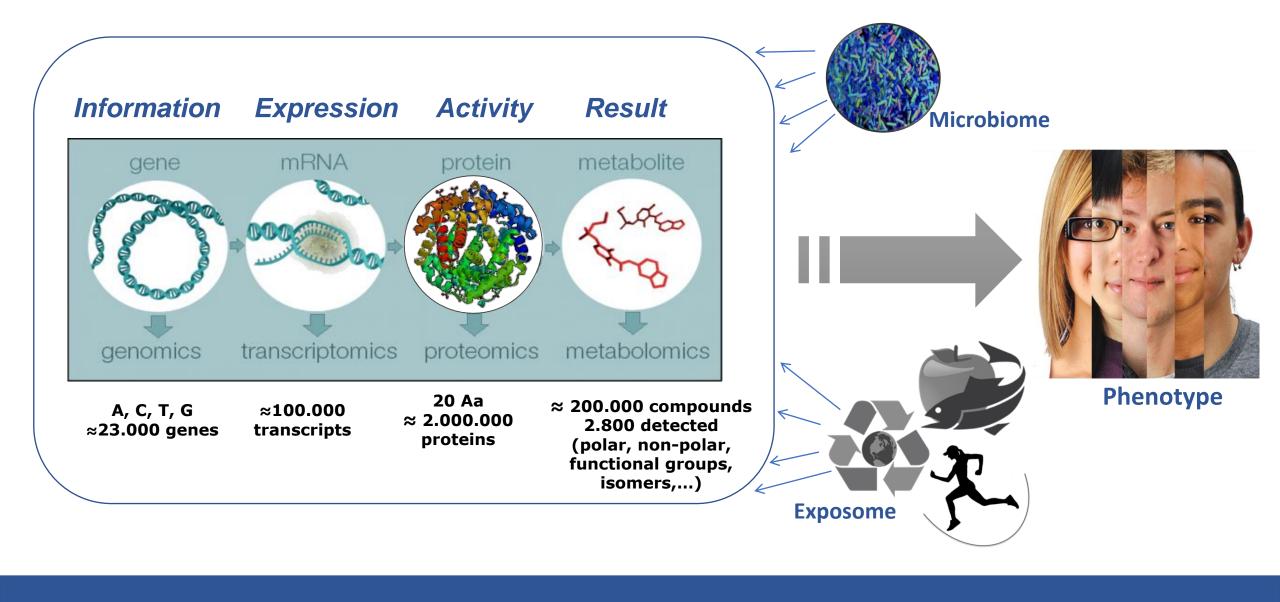
UNIÓN EUROPEA Make the

Make the most out of your omics projects!

www.omicstech.com

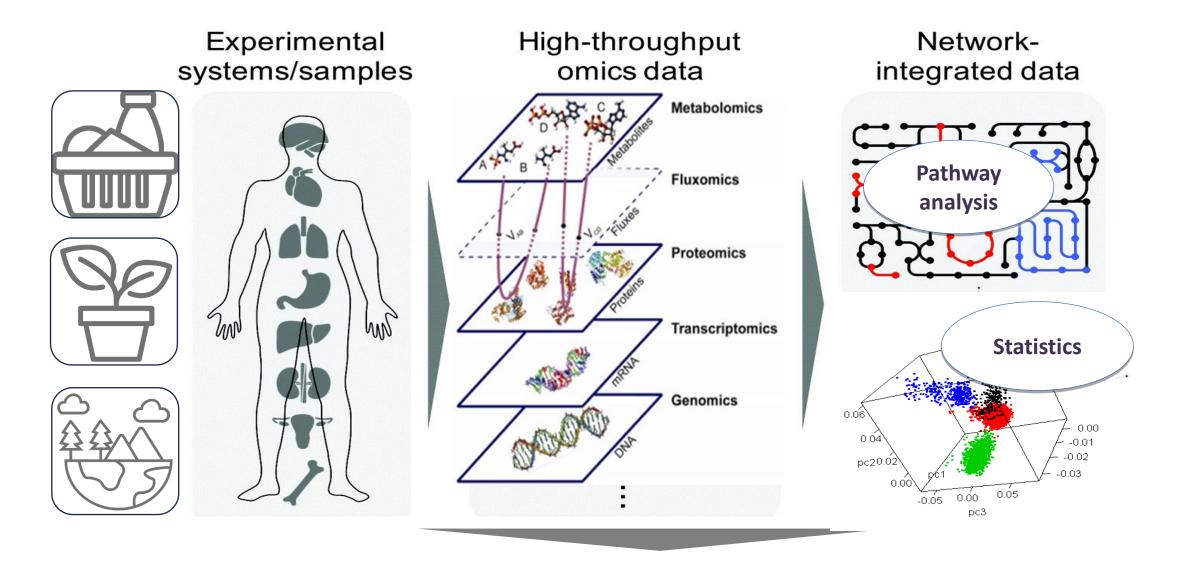
QmicsTech

Types of Omics





Multi-Omics approaches



PREDICTION - DIAGNOSIS - TREATMENT EFFICACY - STRATIFICATION - PERSONALIZATION



Applications of Omics



Medical and Healthcare

- personalized medicine, and health management
- disease mechanisms and diagnosis
- biomarker discovery
- drug discovery and development
- pharmacogenomics



Agriculture and Crop Sciences

- crop improvement
 plant broading
- plant breeding
 gapatic angineer
- genetic engineeringunderstanding plant
- responses to environmental stresses
- improve crops with enhanced traits



Environmental Sciences

- Ecosystems biodiversity
- environmental pollution
- climate change



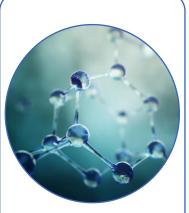
Industrial Fo Biotechnology N

- optimizing industrial bioprocesses
- development of sustainable energy sources and biofuels
- producing bio-based chemicals
- engineering microorganisms for various bioproduction applications



Food and Nutrition

- food safety
- quality control
- nutritional analysis
- understanding foodrelated diseases.
- study foodborne pathogens
- assess nutritional content and bioactive compounds food products



Chemical Industry

- Process Optimization
- Catalyst Development and Screening
- Chemical Safety
 Assessment
- Sustainable Chemistry and Green Processes
- Chemical Analysis and Quality Control
- Bioprocessing and
 Biomanufacturing

Omics approaches provide valuable insights into the genetic and metabolic aspects of chemical processes, enabling more efficient and sustainable production methods



INFRAESTRUCTURAS CIENTÍFICAS Y TÉCNICAS SINGULARES (ICTS)

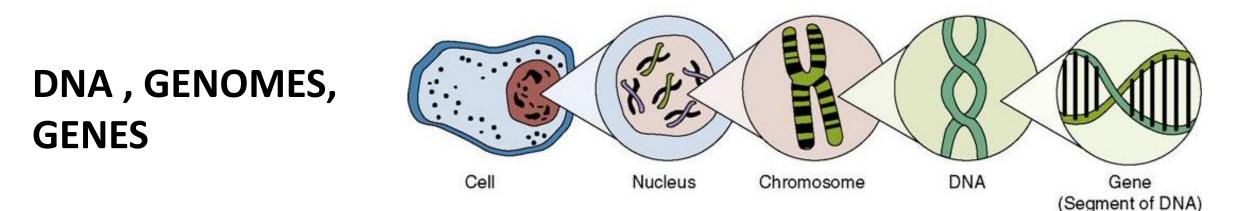


QmicsTech

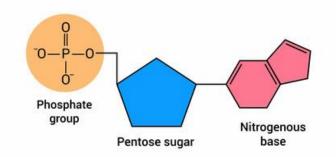




Genomics Area



- ✓ **DNA:** molecule that carries the genetic information.
- One molecule of DNA is made up **nucleotides**: with a sugar group (deoxyribose), a phosphate group and a base. There are four bases: Adenine (A), Thymine (T), Guanine (G) and Cytosine[®].
- ✓ **Genome:** all of the genetic material in an organism
- ✓ Genes: are segments of DNA with the instructions to make specific proteins with specific functions in our body.





Genomics Area

DNA SEQUENCING

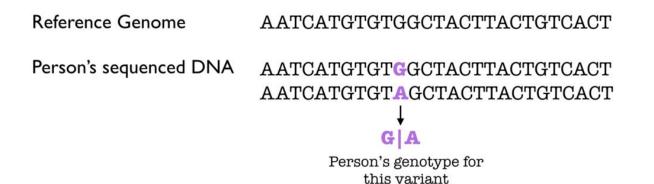
DNA sequencing is the process of determining the nucleic acid sequence, the order of nucleotides (A, T, C, G) in DNA (<u>https://en.wikipedia.org/wiki/DNA_sequencing</u>)

Human genome:

21,000 genes

3,000,000,000 base pairs

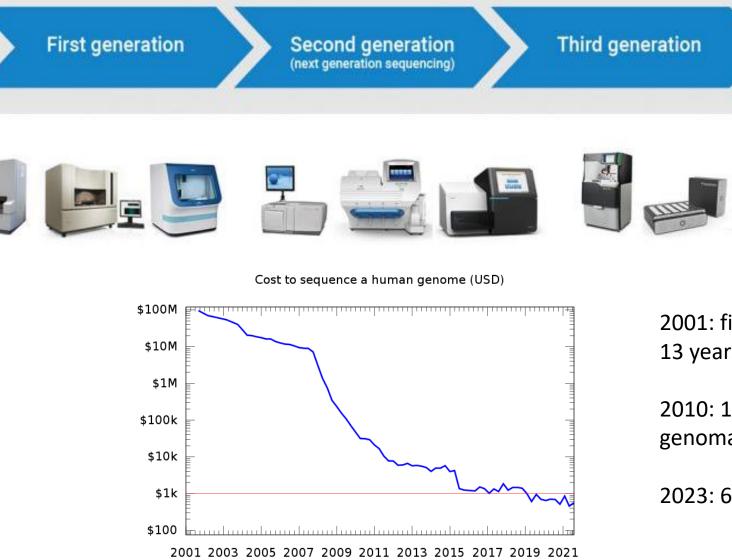
>3,000,000 genetic variants



Some gene variants can cause some genetic diseases or contribute to susceptibility to certain diseases.

OmicsTech

Genomics Area



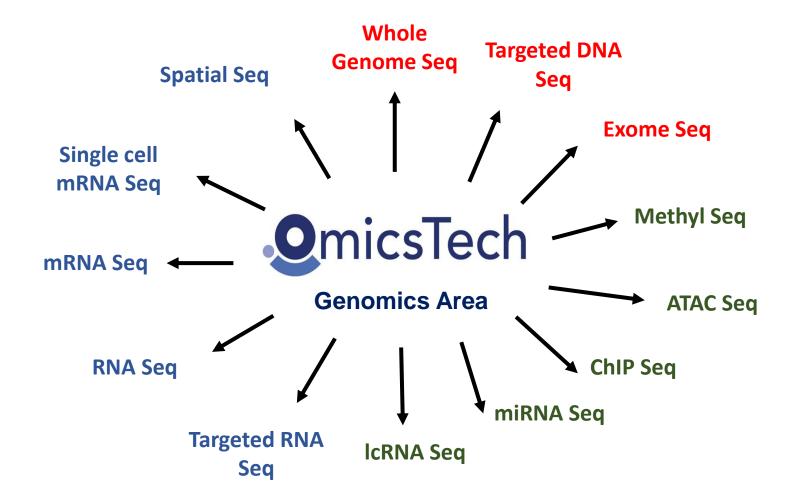
2001: first human genome, 13 years Project, > 100M \$

2010: 15,000 \$/ human genoma

2023: 600 \$/ human genome

OmicsTech

Genomics Area





CENTRO NACIONAL DE ANÁLISIS GENÓMICO (CNAG)

- ✓ Created in 2010
- ✓ 100 people, directed by Ivo Gut
- ✓ Located at the Barcelona Science Park

Mission

To carry out projects in genome analysis that will lead to significant improvements in people's health and quality of life, in collaboration with the Spanish, European and International research and clinical community.

Quality

- ✓ ISO 9001 Certification (Quality management system)
- ✓ ISO 17025 2005 Accreditation (General requirements for the competence of testing and calibration laboratories)
- ✓ ISO 27001 Certification (information security management system)
- ✓ Genomic Quality Assessment Programs (GenQA)

Genomics Area

cnag

centre nacional d'anàlisi genòmica centro nacional de análisis genómico



QmicsTech

Genomics Area



Sequencing instruments

Sequencing capacity

Single cell Genomics

Spatial Genomics

Computing

5 Illumina sequencers (3 NovaSeq6000, 1 HiSeq2500, 1 MiSeq)2 Oxford Nanopore Technologies sequencers (1 Gridlon, 1 Promethion)

>10,000 Gbases/day = 100 human genomes/day at 30x

10x Chromium Controller, 10x Chromium Connect

Vutara microscope CosMX

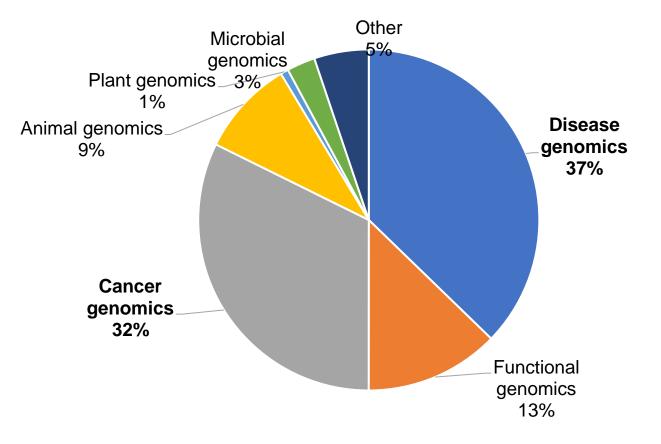
13,000 cores 13 PB disk + 3 PB tape

QmicsTech

Genomics Area

2022 CNAG-CRG activity

- ✓ 1,021 Projects completed
- ✓ 237 Different Users
- ✓ 17,343 Samples processed
- ✓ 486 Terabases of sequence produced
- ✓ 248 Projects analyzed





AREAS OF COLLABORATION WITH BIOMEDICAL SECTOR

Discovery science

- Characterization of disease biology and/or treatment response
- Identification of new targets for drug development
- Biomarker identification and validation
- Characterization of rare cells (circulating tumor cells, immune cells, progenitor cells)

Translational research

 Precision medicine clinical trials with robust genomic patient stratification for increasing drug safety and effectiveness

Clinical applications

- Diagnostics and companion diagnostics
- Pharmacogenomics
- Clinical Decision Support Tool

OmicsTech

Genomics Area

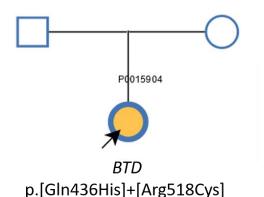
Success story I: Implementation of whole genome sequencing for pediatric cases in the Navarre health care system

Collaboration with Complejo Hospitalario de Navarra

- \checkmark Whole genome sequencing
- ✓ 75 children at Intensive Care Units with suspected genetic disorder
- ✓ Results in 14 days
- ✓ Disease causing mutation identified in 40% cases

Case report

- ✓ 1 month old female newborn with seizures, hypotonia, breathing problems, hearing and vision loss, ataxia, skin rashes, alopecia and candidiasis
- \checkmark Identification of two pathogenic variants in the BTD gene
- ✓ Diagnostic: biotinidase deficiency
- ✓ Treatment: oral biotin





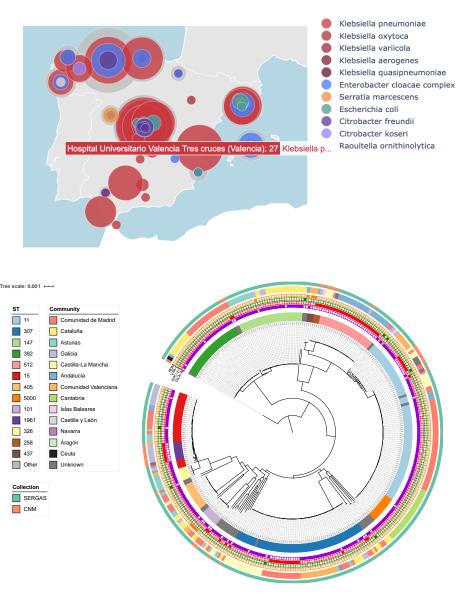
OmicsTech

Genomics Area

Success story II: Studying multi drug resistance bacteria

- Carbapenem-resistant bacteria is an ongoing public-health problem of global dimension
- They produce an enzyme called a carbapenemase that makes antibiotics like carbapenems, penicillins, and cephalosporins ineffective
- ✓ Public-private collaboration (Roche Diagnostics, Universidad de la Coruña, Sociedad Española de Enfermedades Infecciosas)
- ✓ Sequencing the genome of 461 samples of Carbapenemase-Resistant Enterobacteriaceae

✓ **inCREDBle** database for browsing clinical and genomic data.





Genomics Area

AREAS OF COLLABORATION WITH AGRO SECTOR

Discovery science

- Plant and animal biology: understanding the genetic influence on traits and disease.
- Biomarker identification and validation

Applied research

- Inform breeding decisions: genomic selection
- Characterize disease susceptibility
- Biodiversity monitoring



Genomics Area

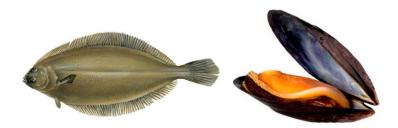
Success story III: Generation of reference genomes of ecologically and socioeconomically important species

De novo assembly of the genome of several species:

- ✓ Senegalese sole (Manuel Manchado, IFAPA)
- ✓ Turbot (Antonio Figueras, CSIC)
- ✓ Mediterranean mussel (Antonio Figueras, CSIC)
- ✓ Phaseolus vulgaris (Roderic Guigó, CRG)
- ✓ Melon (García-Mas, CRAG)
- ✓ Olive tree
- ✓ Silver fir (David B. Neale, UC Davis)

Participation in local and international initiatives in Biodiversity Genomics

- ✓ Earth Biogenome Project (EBP)
- ✓ Catalan Initiative for the EBP (CBP)
- ✓ Vertebrate Genome Project (VGP)
- ✓ Biodiversity Genome Europe (BGE)





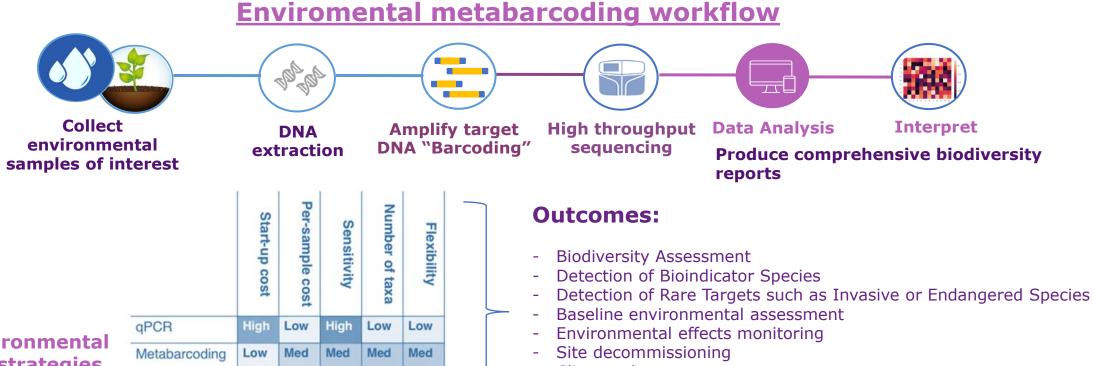




Metabolomics Area

Environmental DNA for impact assessments

Environmental impact assessments are carried out to predict the effects of a particular development project on the natural environment, such as a new mine or new oil pipeline. Next generation sequencing (NGS) allows the massive detection of environmental or eDNA by barcoding techniques together with metagenomics of environmental microbiomes.



- Climate change
- Pathogen detection
- Aquatic, terrestrial, sediments health

Other environmental genomics strategies offered by COS

	Start-up cost	er-sample cost	Sensitivity	umber of taxa	Flexibility
qPCR	High	Low	High	Low	Low
Metabarcoding	Low	Med	Med	Med	Med
Capture	High	Med	Med	High	High
Shotgun	Low	High	Low	High	High



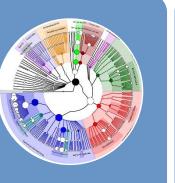
Metabolomics Area

Genomics-based water quality monitoring

DNA-based technologies can quickly and accurately detect pathogens in a water supply, identifying unsafe water before it can make people sick. They allow us to determine the microbiological composition/quality of the wastewater or drinking water produced and distributed.



Generation of fingerprints (sometimes called barcoding or barcodes) of the complete microbial population present in (drinking) water based on Next Generation Sequencing (NGS). With this analyses the effect of disturbances on the fingerprint can be examined and indicator organisms/markers can be characterized.



Metagenomic Analysis of Environmental Water Samples provides insight into microbial responses to environmental changes in a water reservoir.



sequencing, enables to examine the complete genomes of the organisms in a given sample comprehensively to evaluate bacterial diversity, detect microbial abundance and changes in their genes, in various environments.



Develop tools for faster and more comprehensive water monitoring for contaminants of existing and emerging concern such as pathogens and pollutants.



Generate information to optimize the microbial processes in industrial and municipal wastewater treatment.

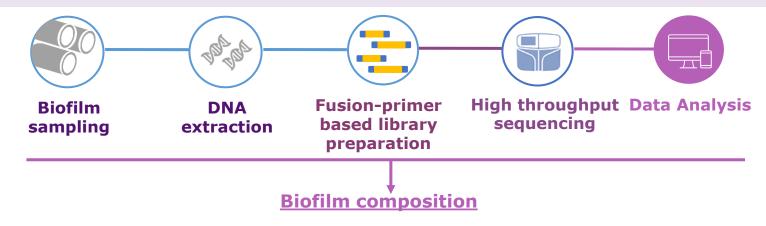


Metabolomics Area

Metagenomics applied to biofilm analyses

Biofilms basically consist of microorganisms embedded in a polymeric extracellular matrix, mostly produced by the organisms themselves. Biofilms are found in several environments, and play both beneficial and detrimental roles depending on whether their formation is controlled, or it occurs naturally

In drinking or industrial water distribution systems, biofilms are the predominant mode of microbial growth, and their formation poses a significant problem to the water distribution network conditions in buildings as a potential source of bacterial contamination, and also affecting the taste and odor of drinking water and promoting the corrosion of pipes.



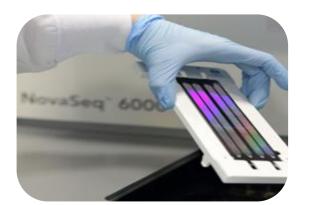
- <u>Untargeted biofilm characterization</u>: determine which microbes (bacteria and fungi) are present, for instance in a corrosion process
- Intermicrobes' interactions: investigate and determine which of the microbes present in the biofilm are active and how they interact with each other
- <u>Omic data generation</u>: Genomic data to develop mathematical models that positively influence predicting the impact and necessity for biocide deployment
- <u>Treatment method efficacy testing</u>: determine the microbial composition of a biofilm before and after mitigation strategies to asses treatment efficacy.



INFRAESTRUCTURAS CIENTÍFICAS Y TÉCNICAS SINGULARES (ICTS)



OmicsTech



Genomics Area CNAG and COS



Proteomics Area CRG and COS



Metabolomics Area COS



Universitat Pompeu Fabra

Barcelona

COS Centre for Omic Sciences eurecat

UNIVERSITAT ROVERALVERGED







FONDO EUROPEO DE DESARROLLO REGIONAL

UROPEAN UNION European Regional Development Fund Jna manera de hacer Europa Make the most out of your omics projects!

www.omicstech.com



PROTEINS



Proteins work together in a coordinated manner to maintain homeostasis and "health"

DRUGS

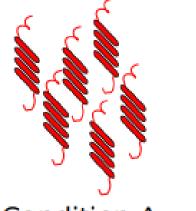
- act on proteins
- are proteins themselves
- lead to the production or degradation of proteins
- use the protein machinery to exert their therapeutic effect

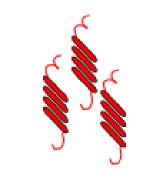
GLP-1 receptor OZEMPIC



Proteomics Applications

Protein abundance changes



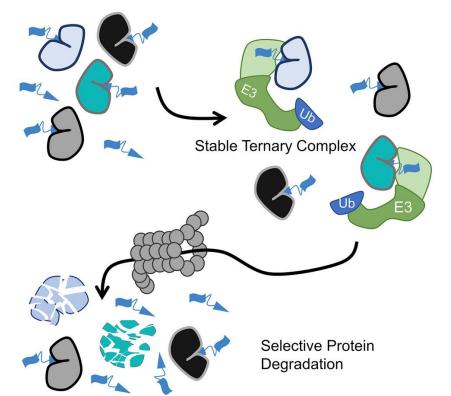


Condition A

Condition B

Examples — Targeted proteome degradation

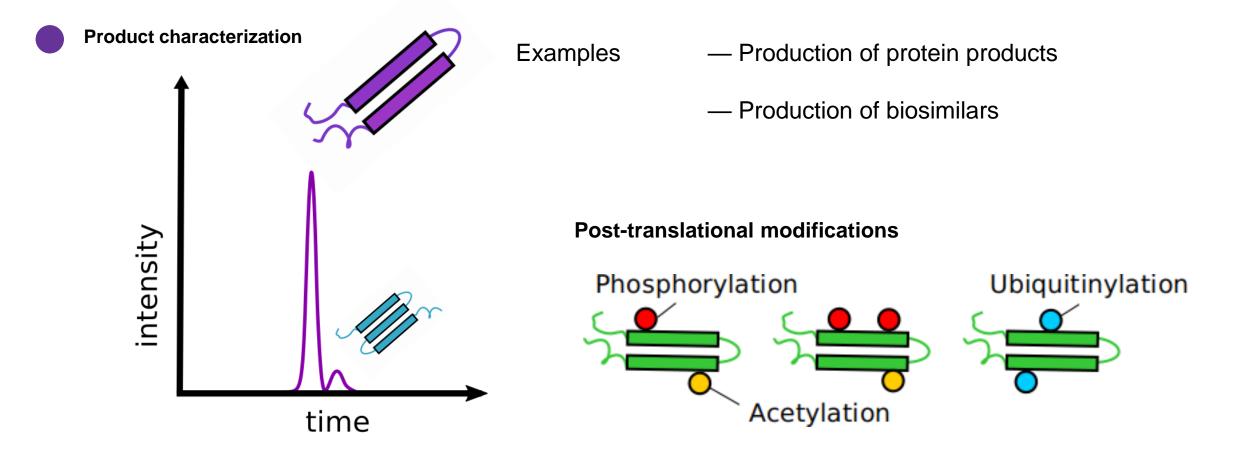
Promiscuous Kinase PROTAC



Bondeson, Daniel P., et al. "Lessons in PROTAC design from selective degradation with a promiscuous warhead." Cell chemical biology 25.1 (2018): 78-87.



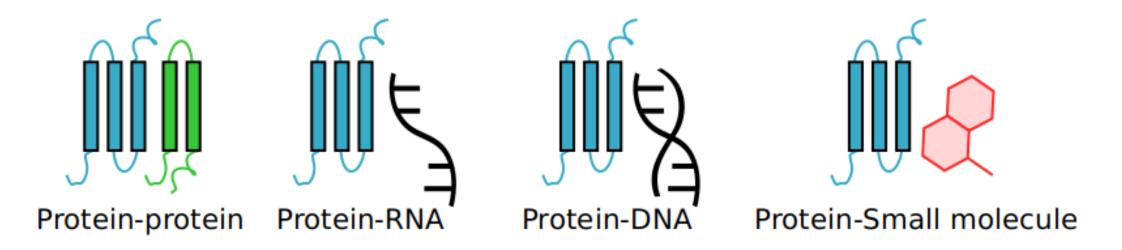
Proteomics Applications





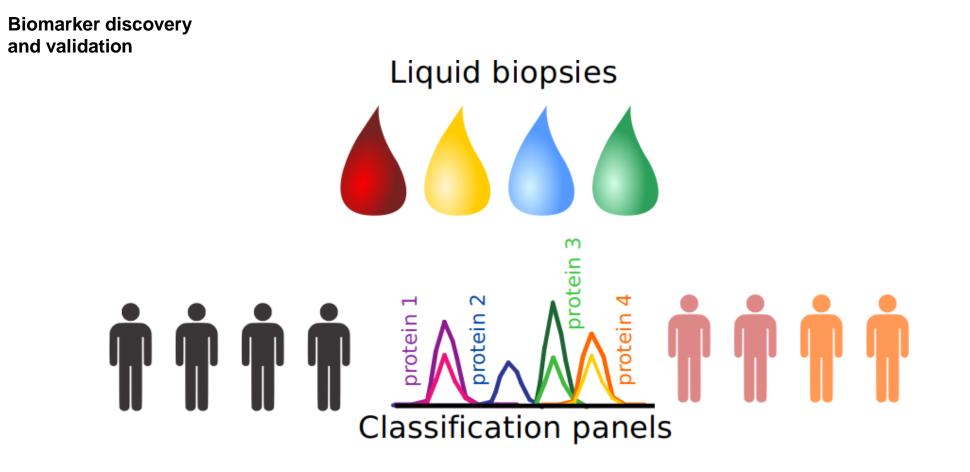
Proteomics Applications

Characterization of protein interactions



Examples — Identification of off-target drug binding







Mass spectrometry-based proteomics

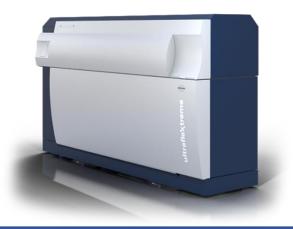














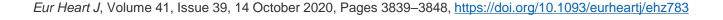
Antobody-based proteomics

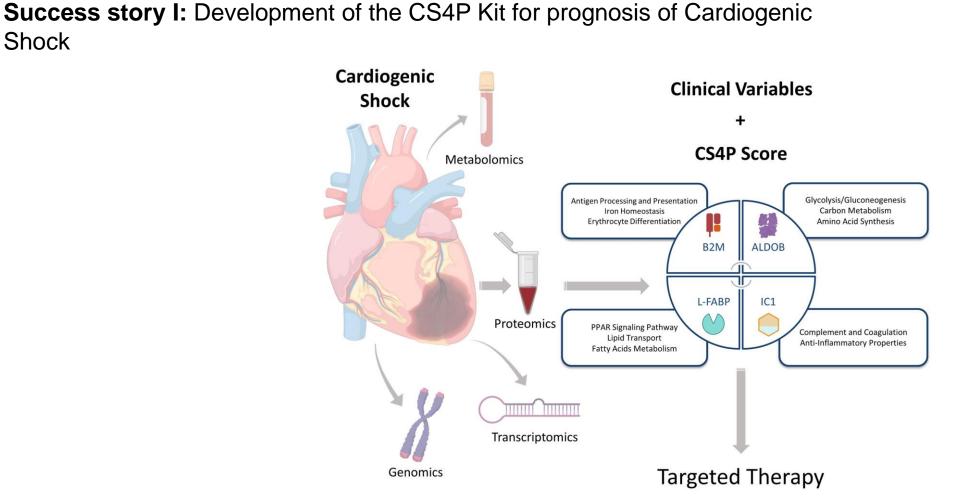
Bioplex 200



Luminex kits MAGPIX









Shock





Dr Toni Bayès

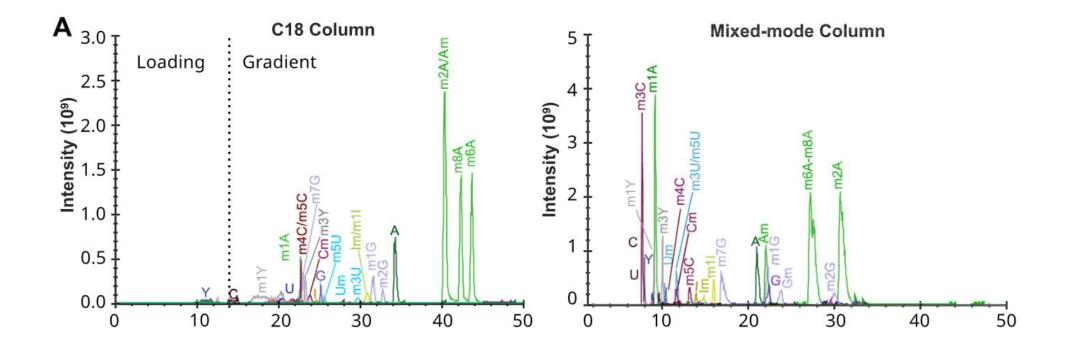
ESC

European Society

of Cardiology



Success story II: High-performance nano-flow liquid chromatography column (RNA nucleosides)



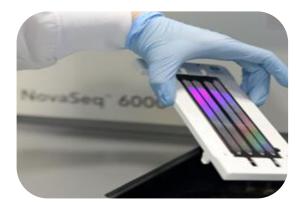




INFRAESTRUCTURAS CIENTÍFICAS Y TÉCNICAS SINGULARES (ICTS)



QmicsTech



Genomics Area CNAG and COS

cnag

centre nacional d'anàlisi genòmica centro nacional de anàlisis genòmico



Proteomics Area CRG and COS



Metabolomics Area COS









UNIVERSITAT ROVERALVERGED





EUROPEAN UNION
 European Regional
 Development Fund
 "Una manera de hacer Europa

FONDO EUROPEO DE DESARROLLO REGIONAL

UNIÓN EUROPEA

Make the most out of your omics projects!

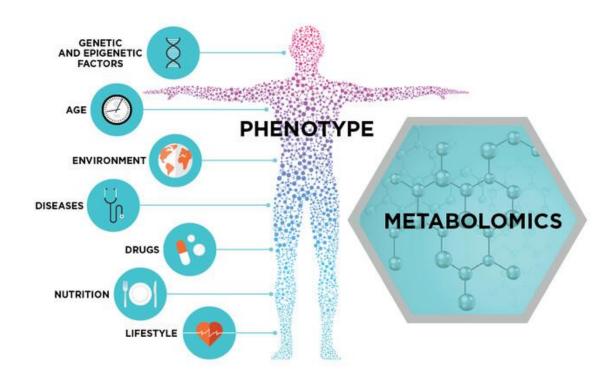
www.omicstech.com

OmicsTech

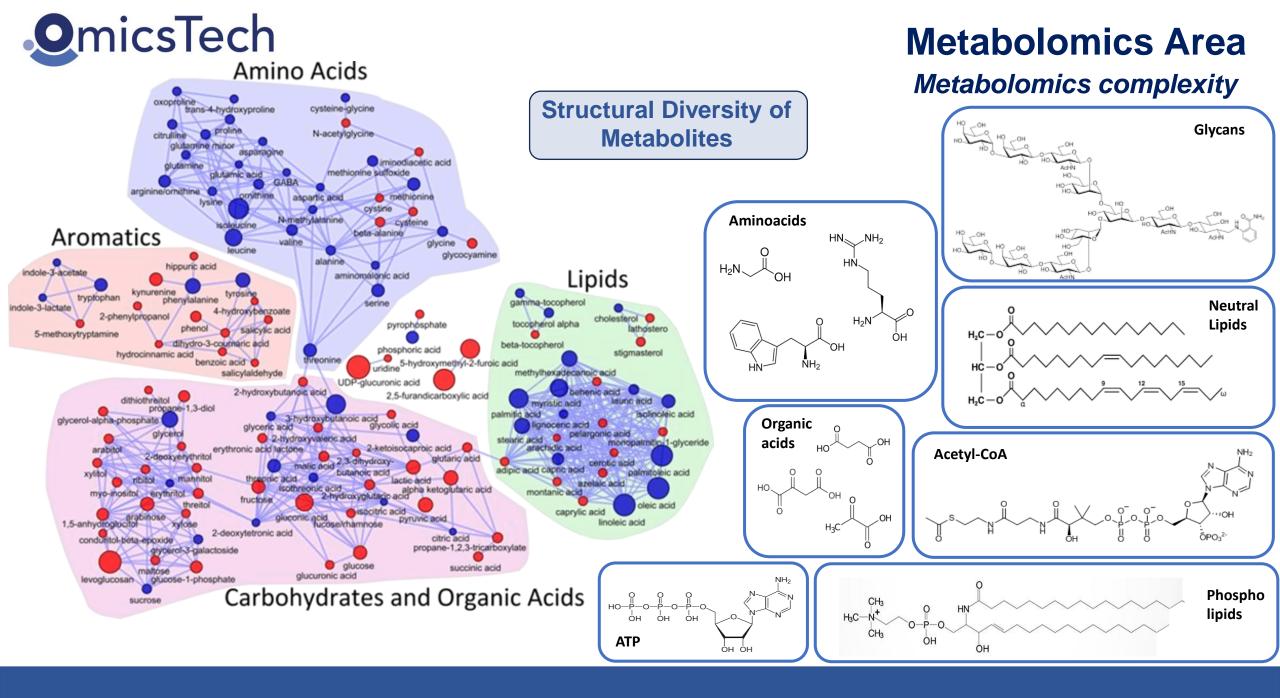
Metabolomics Area

Metabolomics concepts

- Metabolomics is the measurement and quantitation of small molecules (< 1500 Dalton). The Metabolome study.
- A metabolite is the intermediate or the end product of metabolism, and they have many functions such as energy, structural, signaling, catalytic activity, defense and interactions with other organisms.
- Small molecules may be endogenous compounds involved in cellular metabolism, although they may also come from drugs, food, microbes or the environment.
- Analysis of an individual's metabolic status leads to personalized medicine and nutrition, the discovery of pathology-related pathways, and new diagnostic and prognostic biomarkers.

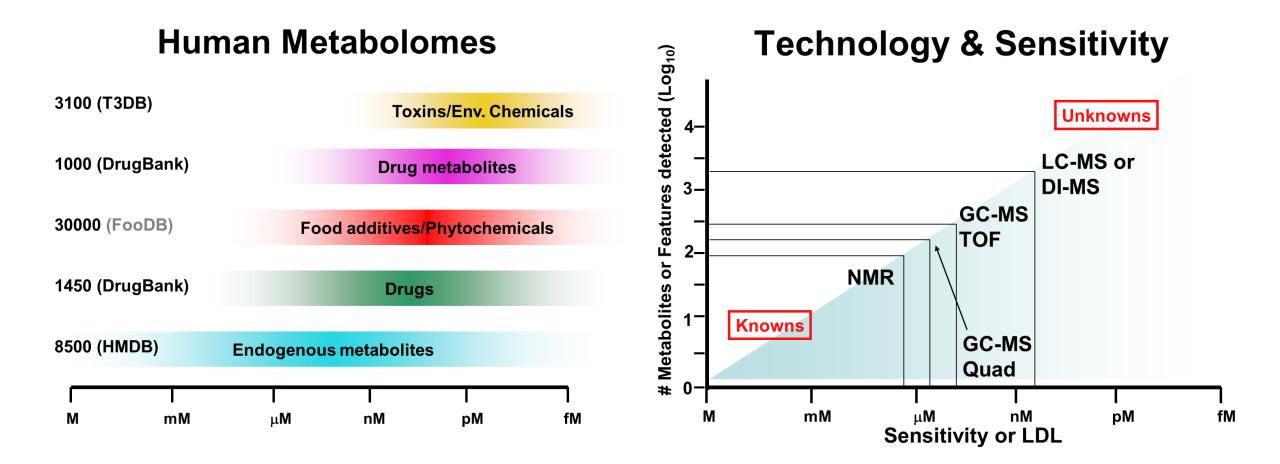


"The metabolites provide us with direct measures of the effects that genetic and lifestyle factors can have on the phenotype"



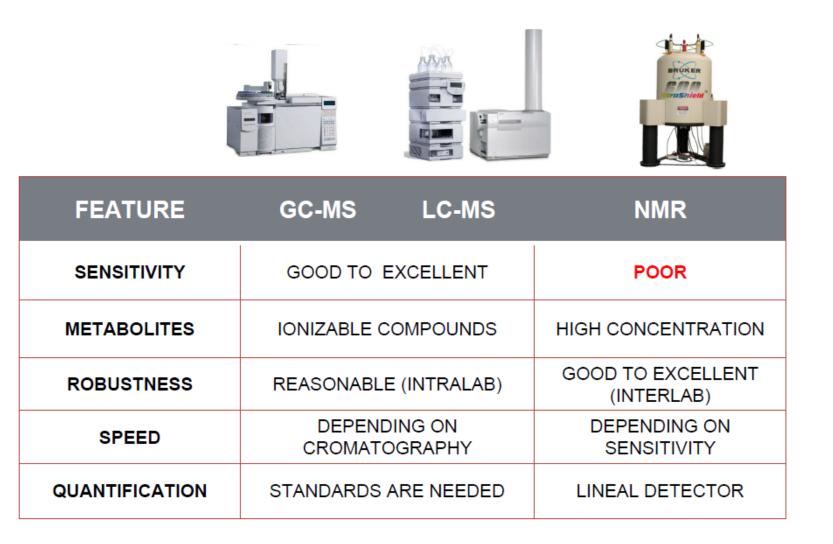


Metabolomics complexity



Metabolomics Area

Analytical platforms



Agilent 6470 Triple Quadrupole LC-MS/MS Agilent 6490 Triple Quadrupole with iFunnel technology LC-MS/MS Agilent 6490 Triple Quadrupole with iFunnel technology LC-MS/MS

Agilent 7000 Triple Quadrupole GC-MS/MS Agilent 7010 Triple Quadrupole GC-MS/MS

Agilent 6550 Quadrupole Time of Flight with iFunnel technology LC/MS Agilent 6546 Quadrupole Time of Flight LC/MS

Agilent 7200 Quadrupole Time of Flight GC/MS Agilent 7250 Quadrupole Time of Flight GC/MS

LECO Pegasus 4D GCxGC-TOFMS

Thermo Orbitrap Velos Pro Thermo Orbitrap Eclipse Tribrid

Bruker MALDI-TOF/TOF UltrafleXtreme

Bruker 400 Hz Nuclear Magnetic Resonance (NMR) Bruker 600 Hz Nuclear Magnetic Resonance (NMR)

Gilson System for automated liquid handling Agilent Bravo liquid handling system Agilent Bravo liquid handling system

Metabolomics Area

Analytical platforms



Thermo Scientific[™] Orbitrap Eclipse[™] Tribrid[™] mass spectrometer



Orbitrap Eclipse, is an instrument designed to address the most difficult analytical challenges, providing accurate and high-throughput full-metabolome or proteome quantitation, characterization of complex mixtures of protein or small molecule-based pharmaceuticals, and deciphering higherorder protein structures.

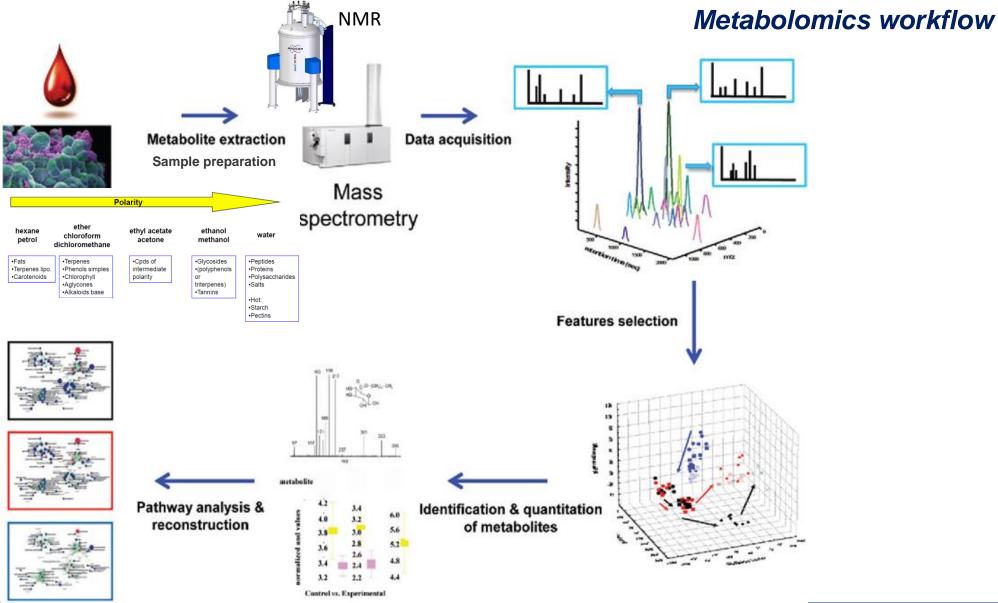


Metabolomics Area Analytical platforms

- Advanced Ion Management Technology (AIM+)
- Exceptional precursor selectivity and sensitivity with the nextgeneration quadrupole mass filter QR5
- Unmatched depth and accuracy of TMT analysis with novel Real-Time Search
- High Mass Range MSn (HMRn) option for comprehensive analysis of native protein complexes
- Unique Proton Transfer Charge Reduction (PTCR) option for simplifying complex top-down spectra
- Enhanced Vacuum Technology
- Full experimental flexibility with revolutionary instrument control
- A wide range of optional functionalities for unprecedented versatility
- Common user interface with Thermo Scientific[™] Orbitrap Exploris[™]
 480 and TSQ[™] triple quadrupole mass spectrometers

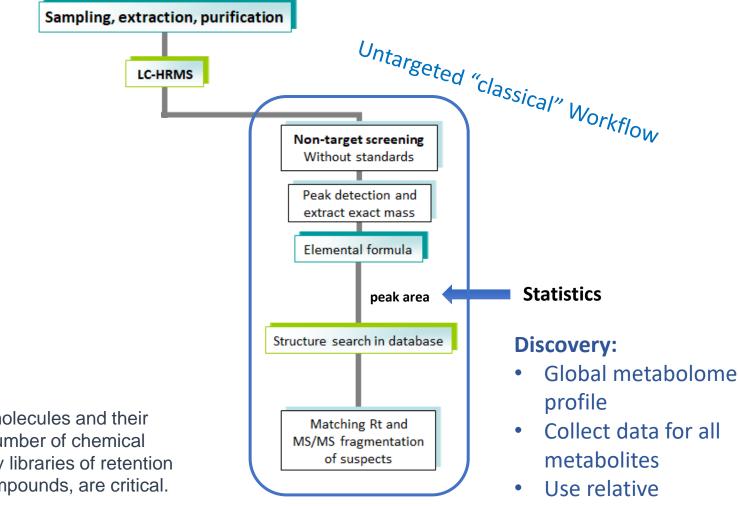
QmicsTech

Metabolomics Area



Metabolomics workflow

quantification

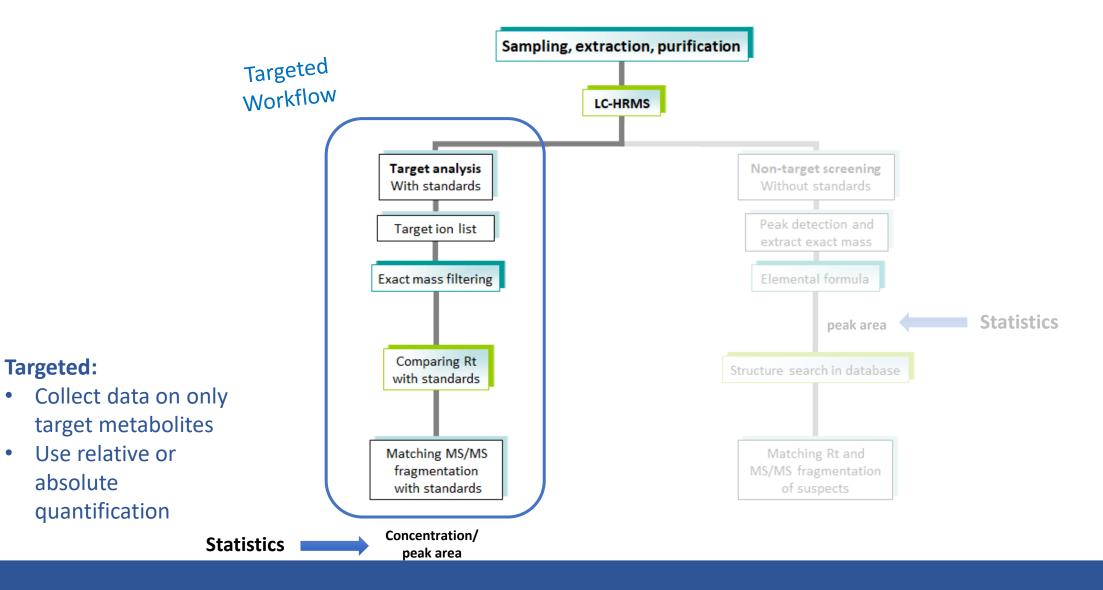


Unfortunately, knowing only the exact masses of molecules and their fragments is not enough to identify them. Huge number of chemical structures can have the same exact mass. This is why libraries of retention times and mass spectra, determined for standard compounds, are critical.

OmicsTech

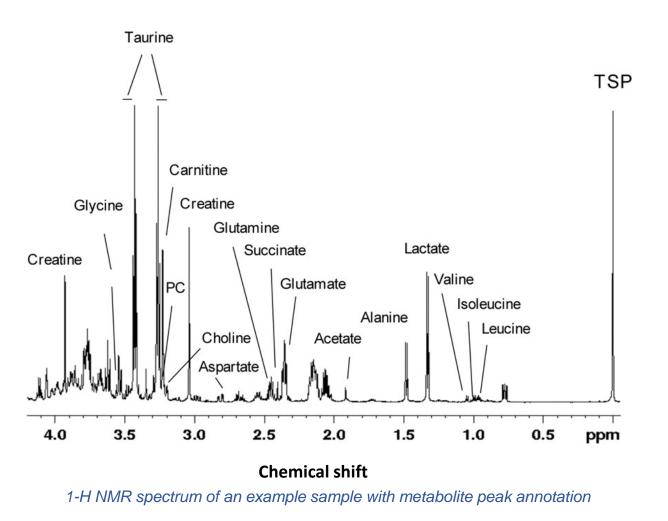
Metabolomics Area

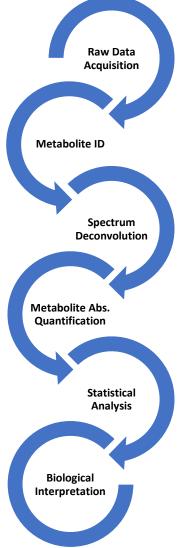
Metabolomics workflow



Metabolomics Area

¹H-Nuclear Magnetic Resonance (NMR)





NMR does not destroy the sample

NMR can detect and <u>quantify</u> metabolite because the signal intensity is only determined by the molar concentration

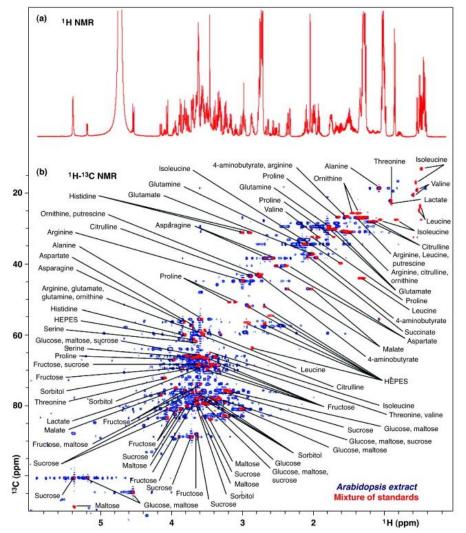
The main weakness of NMR is <u>low sensitivity</u> relative to MS. ¹H is more sensible than ¹³C

NMR can provide comprehensive structural information, including stereochemistry

Many atoms have nuclei that are NMR active, but most NMR data are collected for ¹H and ¹³C since these are present in all organic molecules

Metabolomics Area

¹H-Nuclear Magnetic Resonance (NMR)



HSQC used to select for protons directly bonded to 13C.

Use of HSQC spectroscopy for analysis of common metabolites. In 1D spectra, overlapped signals hamper identification of individual metabolites, whereas in 2D correlation, spots are easily visible.

Signal overlap is a problem in the complex spectra of plant extracts. Signal overlap hampers metabolite identification and quantification. Better signal resolution can be obtained using various types of 2D NMR spectroscopy. These approaches cut signal overlap by spreading the resonances in a second dimension.

(a) 1D 1H NMR spectrum of an equimolar mixture of the 26 standards.

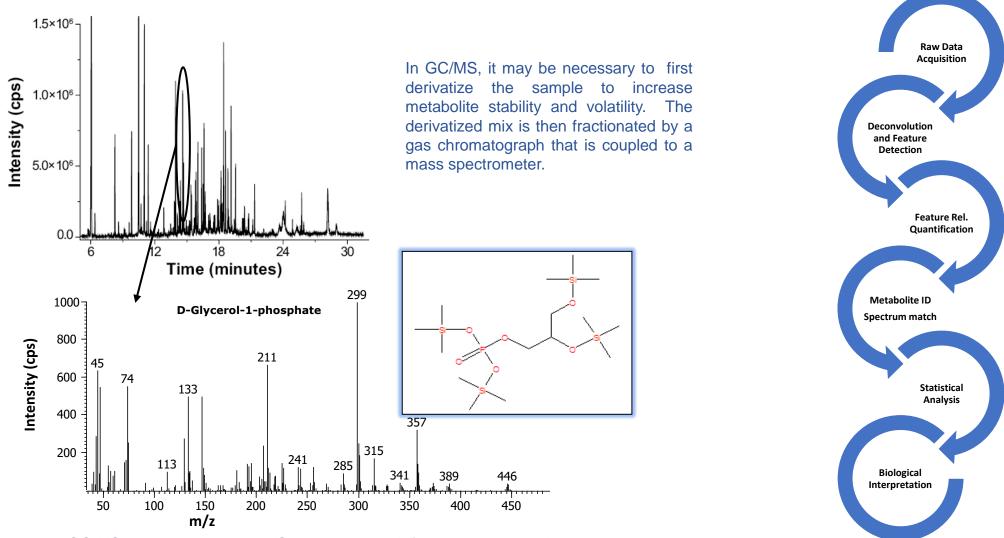
(b) 2D 1H–13C HSQC NMR spectra of the same synthetic mixture (red) overlaid onto a spectrum of aqueous whole-plant extract from Arabidopsis (blue).

PMID: 21435731

2D ¹H -13C NMR spectrum of an example sample with metabolite peak annotation



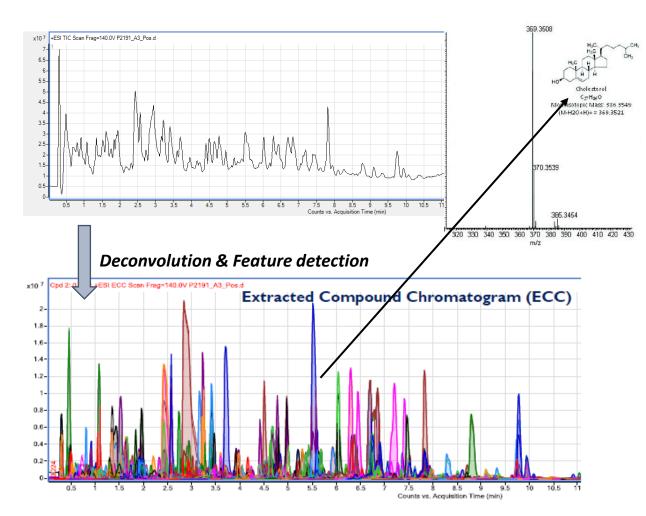
GAS CHROMATOGRAPHY – MASS SPECTROMETRY (GC-MS)



GC-MS chromatogram and MS spectrum match for a selected metabolite



LIQUID CHROMATOGRAPHY – MASS SPECTROMETRY (LC-MS)

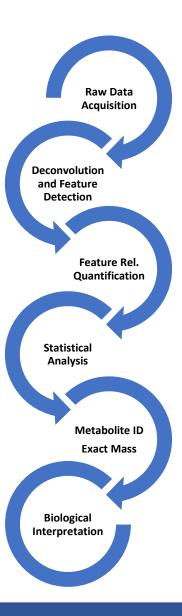


LC-MS chromatogram, Features detected and HRMS spectrum for a selected metabolite

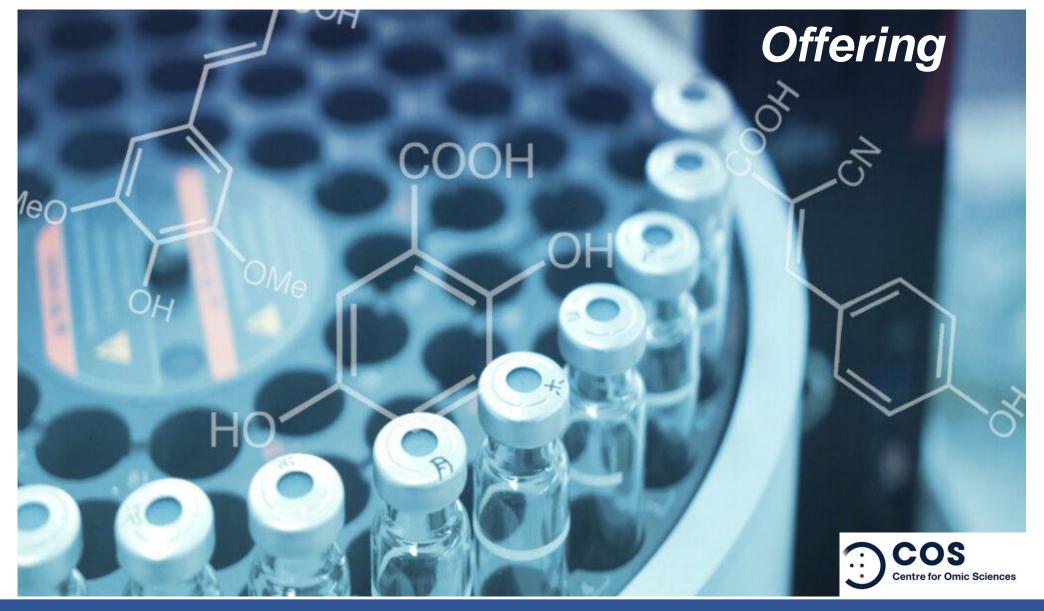
In LC/MS (also termed high performance liquid chromatography, HPLC/MS) the samples are not derivatized before analysis and an HPLC instrument is used for separation.

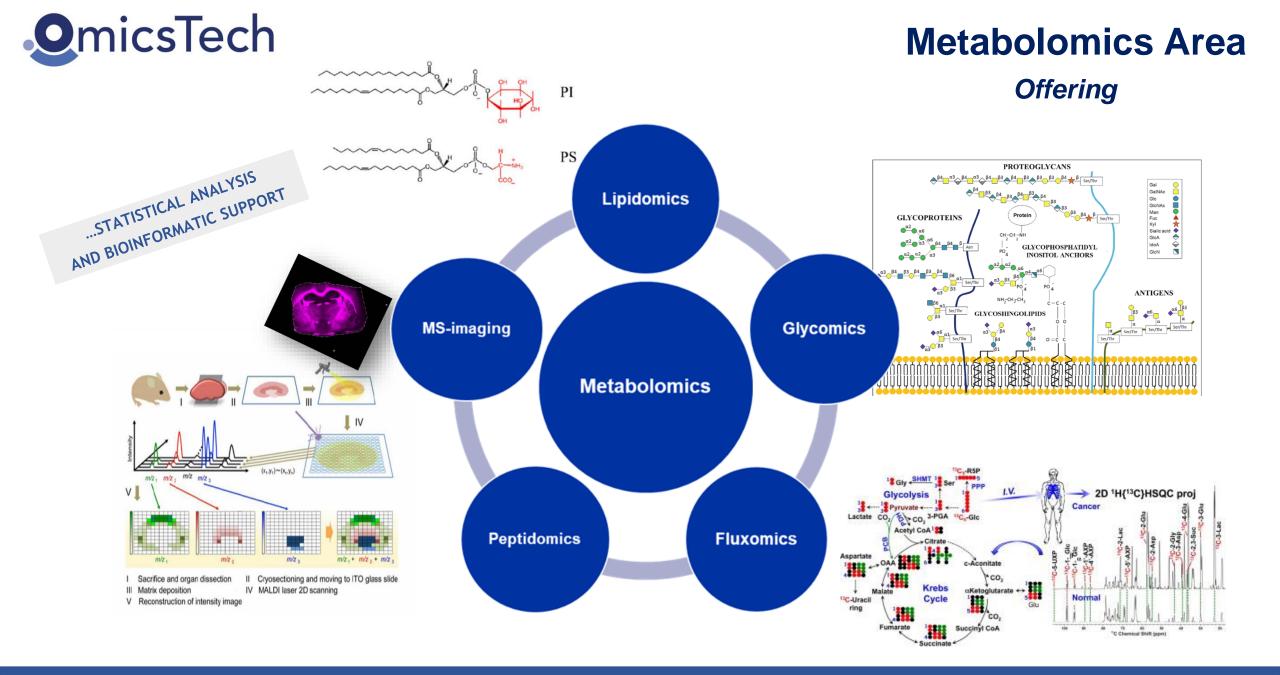
LC/MS is more suitable than GC/MS for labile compounds, for those that are hard to derivatize, or hard to render volatile.

LC/MS is less developed than GC/MS. A closely related method is capillary electrophoresis (CE)/MS.









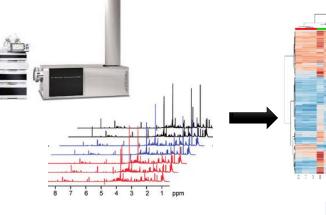
QmicsTech

Metabolomics Area

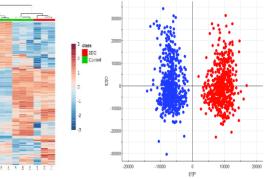
Untargeted omics aproach



aims for a quick and reliable identification of small molecule biomarkers characteristic for a particular **physiological state**



Biomarker discovery



Multivariate Data analysis

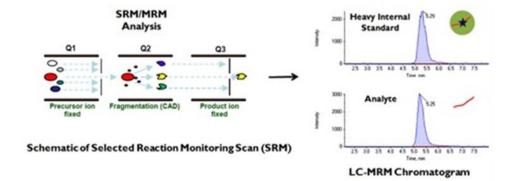
Targeted omics approach



Validate **biomarke**r candidates and analyze known target compounds

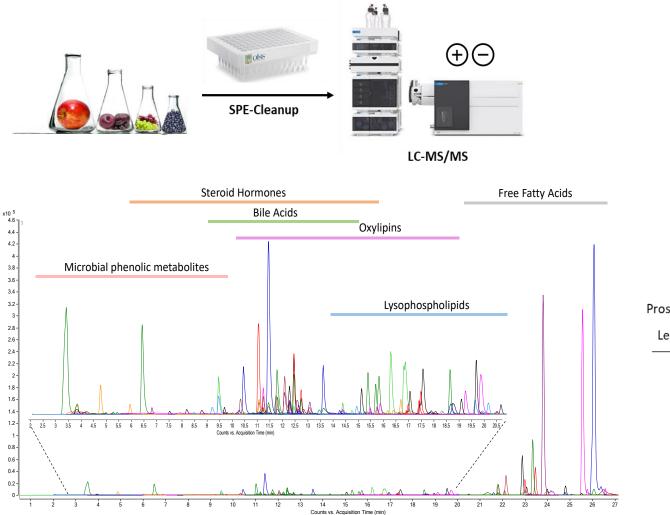
- Amino Acid Extend
- Acylcarnitine
- Bile Acids
- Short Chain Fatty Acids
- Oxylipins
- Polyamines
- Methylamines
- Energy Metabolism
- Fatty Acids
- Customized analysis

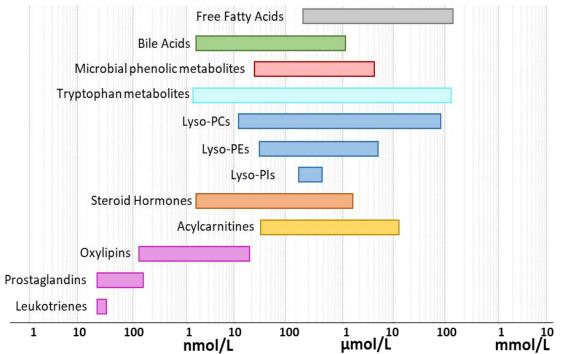
Biomarker Valiation/Quatification





Metabolomics Area Lipidomics

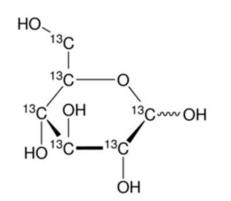




QmicsTech

Metabolomics Area

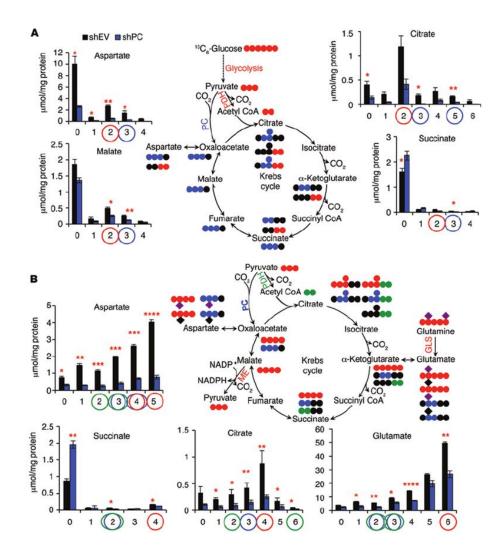
Fluxomics



Fluxomics describes the various approaches that seek to determine the **rates of metabolic reactions** within a biological entity

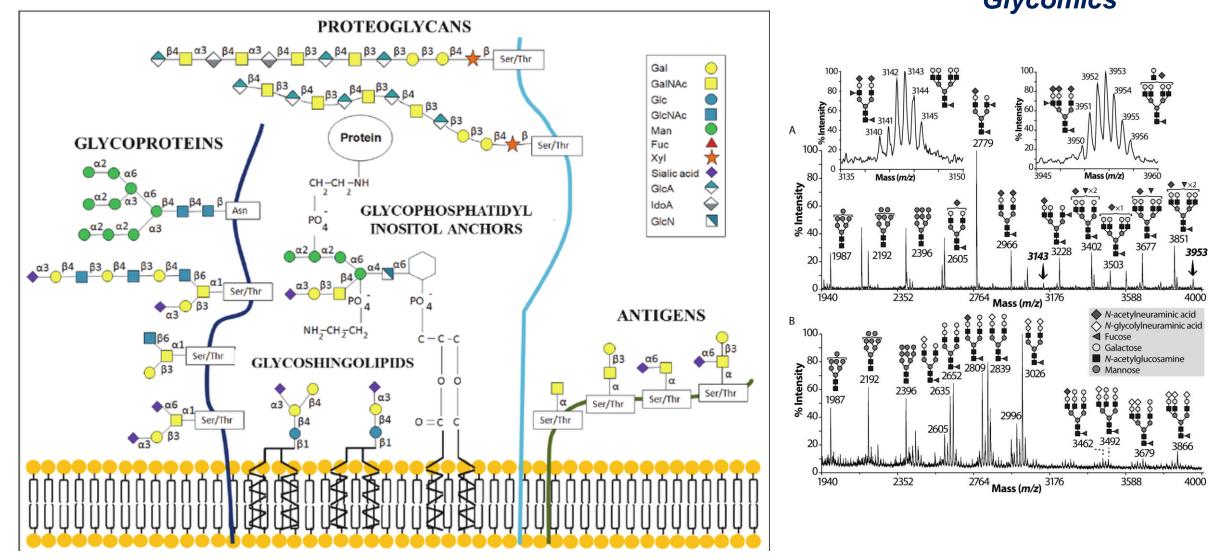


In 13C-fluxomics, metabolic precursors are enriched with 13C before being introduced to the system





Metabolomics Area Glycomics



Metabolomics Area

MS-Imaging

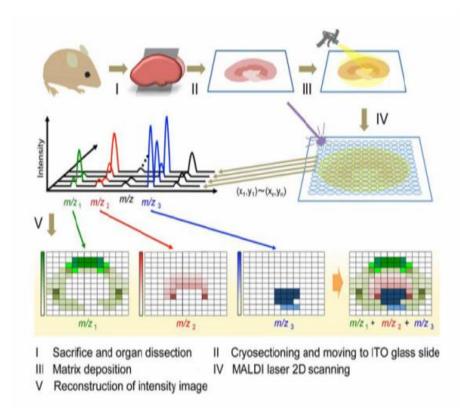


Figura 1. Flux de l'anàlisi mitjançant MALDI-MSI

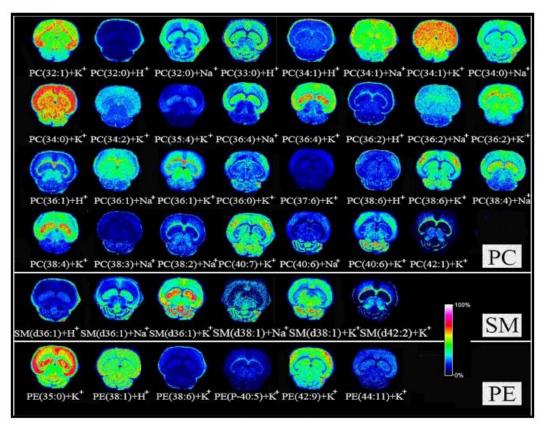


Figura 2. Distribució de lípids en seccions de cervell de rata. PC: fosfatidilcolines, SM: esfingomielines, PE: fosfatidiletanolamines [16]





ALTERNATIVE

Metabolomics Area

Organ on a chip, Omics, Machine Learning

Environmental Toxicity chemical mixtures through an innovative platform based on aged cardiac tissue model

Platform to detect the cardiotoxicity of chemical substances and their biotransformation products that will allow to identify, quantify and prevent multiple cardiotoxic exposures to chemical and pharmaceutical products.

The project is focused on the cardiotoxic effects in the great people

The platform will consist of an in vitro three-dimensional heart rate engineering model (OCC) that will imitate the heart rate of young and aged humans, together with a monitoring system based on multichemical analysis and integrated into a learning risk assessment queen automatic (ML).

It allows to evaluate the unpredictable toxicity due to the synergic effects of different chemical substances, added by the human envelopment process.

The combination of an in vitro cardiac system and ML models will reduce and replace the need for animal testing.

H2020 GREEN DEAL Consortium: 11 Parthners. Leader Politecnico di Torino

Precision

OmicsTech

fermentation

Super-producing bacterial cultures to improve the performance of the production of biodegradable plastics, biofuels, drugs, nutrients,...

Precision fermentation: we are working on altering the genome of different microorganisms through gene editing via CRISPR/cas9 to improve the production of microbial enzymes.

Some parameters of the bacterial cultures need to be optimized such as pH, temperature, enzyme concentration, substrate concentration, reaction time and for this, modifications can be made at the genetic level to manipulate the enzymes and promote an increase in the yield of its activity, generating a higher yield in obtaining the product, with higher quality.

Application of biotechnology in organic waste treatment processes on an industrial scale to obtain bioplastics, biofuels, nutrients,...

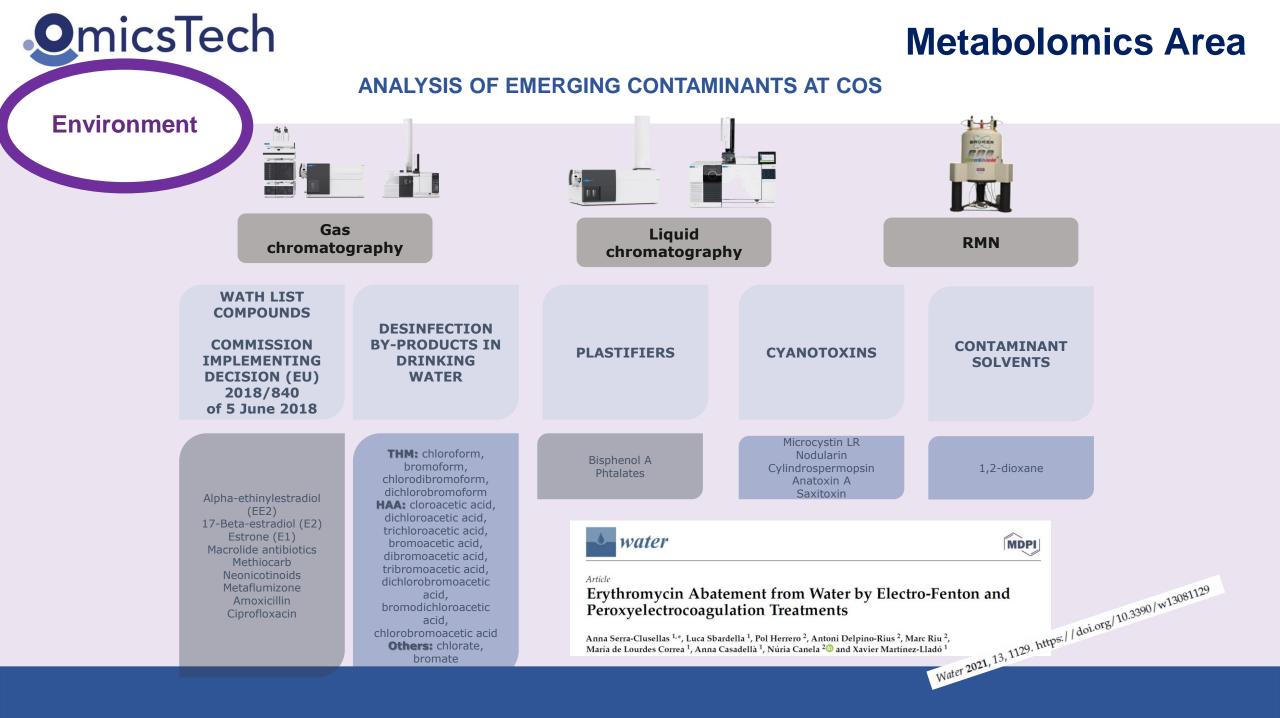
Environment

OmicsTech

Water Organic Contaminants Analyses

- Over 1,000 toxic chemicals, pesticides, and pathological organisms may be into our drinking water because of human behaviors. Based on experience on water quality analysis and a state-of-the-art metabolomics platforms containing sensitive and accurate liquid and gas chromatography coupled to mass spectrometry instruments, COS can provide services to help you with water quality analysis.
- Emerging pollutants: pollutants that are currently not included in routine monitoring programmes at the European level and which may be candidates for future regulation, depending on research on their (eco)toxicity, potential health effects and public perception and on monitoring data regarding their occurrence in the various environmental compartments.
- > For many compounds, no analytical methods are available and no analytical standards





Metabolomics Area

glimicave

Omic Data analysis Global omic data integration on animal, vegetal and environment sectors

Platform based on Big Data (BDA) and artificial intelligence (AI) techniques, integrating pre-existing omic data sets into databases, literature, and experimental data.

- The main result will be a multi-omic data analysis tool applicable to different domains.
- It is hoped to improve the understanding of biological systems by going beyond current databased tools in the industry.

3 industrial sectors: animal production, agriculture and water treatment.



Horizon 2020 European Union funding for Research & Innovatior

https://glomicave.eu/

15 partners/ 6 countries Coordinator: EURECAT - COS

