Photo: Exposoma, Iolanda Filella Cubells. Institut d'Estudis Catalans

Barcelona Exposome Symposium

Abstract book

📅 25/ 09/24
🕐 9.30 - 16.40 h
📍 PRBB, Barcelona

Welcome

Dear Colleagues,

On behalf of the Organizing Committee, it is our great pleasure to welcome you to the Barcelona Exposome Symposium 2024. This event aims to facilitate the sharing of knowledge, ideas, and resources within the exposome research community in the Barcelona area. Whether you're a seasoned exposomics researcher or a newcomer to the field, this symposium invites you to join us in building a supportive community dedicated to advancing exposome research.

The exposome represents the comprehensive set of environmental exposures that an individual encounters throughout their life. Exposomics aims to evaluate how these exposures impact biology and health through discovery-based analytical approaches. This symposium will provide a panorama of exposome research across different institutions in the Barcelona area, with a series of invited presentations, abstract-selected talks, and posters.

This local-level symposium is part of a larger initiative to build an International Human Exposome Network, and we are excited to cover a wide range of topics, including:

- Technological Innovations and Methodologies in Exposomics: We will explore innovations in non-targeted chemical exposome characterization, advancements in computational methods and big data applications, new biomarker development, and geospatial modeling.
- Exposome and Human Health: Research on early-life exposures, chronic diseases, precision medicine, and the role of cumulative environmental exposures in health outcomes will be key topics of discussion.
- Biological Impacts and Experimental Modeling in Exposomics: Discussions will include how environmental exposures influence molecular and cellular processes, integrative omics approaches, and experimental modeling.
- Translational Research: We will explore how experimental findings are being translated into clinical and epidemiological studies to better understand the health implications of the exposome.

This symposium would not have been possible without the collaboration and dedication of several institutions in Barcelona, including ISGlobal's Exposome Hub, CSIC, the University of Barcelona, and EMBL - Human Ecosystems. We are proud to host an event that reflects the cutting-edge research being conducted in our region and beyond.

We also wish to express our sincere gratitude to all the presenters, sponsors, and volunteers who have helped make this event possible. Your participation is key to the success of this symposium, and we look forward to a day filled with insightful discussions and collaborative opportunities.

Thank you for joining us, and welcome to the Barcelona Exposome Symposium!

Warm regards,

Léa Maitre

Assistant Research Professor, ISGlobal, Barcelona
*Exposome Hub coordinator*

Coordinated by:

Support provided by:

Scientific Core Committee

▶ <u>ISGlobal - Exposome Hub</u> (Léa Maitre, Martine Vrijheid, Mariona Bustamente)

▶ <u>CSIC - Institute of Environmental Assessment and Water Research</u> (Pablo Gago-Ferrero)

▶ <u>University of Barcelona - Biomarkers & Nutritional and Food Metabolomics Group</u> (Cristina Andres-Lacueva)

▶ <u>University of Barcelona - Artificial Intelligence in Medicine Lab</u> (Karim Lekadir)

▶ <u>EMBL, Barcelona -</u> Human Ecosytems (Talya L. Dayton)

Agenda
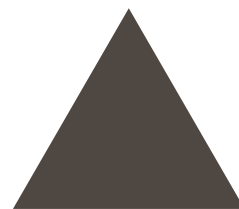
Wednesday, 25th September 2024
9.30h to 16.40h (CET) meeting

9.30-10.00   Opening Remarks by Léa Maitre, Symposium Chair. Overview of the symposium's goals, schedule, and the importance of exposome research.

Introduction to the Local and Global Exposome Research Landscape by Martine Vrijheid, ISGlobal. Discussion on the current state of exposome research, including international projects like IHEN, and key local initiatives.

10.00-10.30   **Keynote 1:** *Advances in Measuring Environmental Exposures in Biological Samples and Their Epidemiological Implications.* **Montse Marquès Bueno, Universitat Rovira i Virgili. Chair: Pablo Gago-Ferrero - CSIC - Institute of Environmental Assessment and Water Research; co-chair Emily Laveriano, ISGlobal.**

10.30-11.10   **Oral presentations - Technological Innovations and Methodologies in Exposomics**

(10min presentation + 2min Q/A)

Selected talks

- *Evaluating Long-Term Exposure to Endocrine Disruptors: A Comparative Study of Hair, Blood, and Urine Samples.* Ana   González-Ruiz, IISPV.

- *Metabolomic biomarkers for dietary fibre exposure: summary from human studies.* Andrea Unión Caballero, UB.

- *Exploring the Chemical Exposome in Brain Cancer: A Proof of Concept.* Daniel Gutiérrez Martín, IDAEA-CSIC.

11.10-11.45   *Coffee break – poster session*

11.45-12.25   **Oral presentations (continued)**

- Assessment of potentially hazardous chemicals during pregnancy. Esteban Restrepo-Montes, CID-CSIC.

- Exposome in Nutrition and Personalized Medicine. Multi-targeted quantitative platform for exposome-based metabolomics. Meryl Cruz, UB.

- Pregnant and lactating women facing climate emergency in Barcelona: an anthropological approach to the environment and perinatal health. Anna Molas and Ana Cerezuela, AFIN-UAB.

12.25-13.00   **Flash talks – 5 min. each – Chair: Karim Lekadir, University of Barcelona - Department of Mathematics and Computer Science; co-chair: Donato Romano, University of Bari/ISGlobal**

Selected talks

- Impact of fatty acid patterns on adolescent neurocognitive function: Insights from neuropsychological assessments. Nicolas Ayala Aldana, ISGlobal.

- Simultaneous determination of neonicotinoid, carbamate/thiocarbamate, triazole, organophosphate and pyrethroid pesticides and their metabolites in urine from general population. Joan Grimalt, IDAEA-CSIC.

- Advanced analytics in pediatric exposomics: Decoding the chemical exposome through machine learning. Mahsa Naghavi Sheikholeslami, IISPV.

- Green space exposure and blood DNA methylation at birth and in childhood – A multi-cohort study. Sofía Aguilar Lacasaña, ISGlobal.

- HYPIEND Digital Tool: A Personalised Platform for Reducing EDC exposure. Laura Sistach, Eurecat.

13.00-14.15   *Lunch / networking - poster session (presenters should be by their posters 13.45 to 14.15)*

14.15-14.45   **Keynote 2:** *The Barcelona Brain Health Initiative (BBHI) - A Cohort Study to Define and Promote Determinants of Brain Health.* **Javier Solana Sánchez, Institut Guttmann. Chair: Cristina Andres-Lacueva - University of Barcelona - Biomarkers & Nutritional and Food Metabolomics Group; co-chair Mariona Bustamante, ISGlobal.**

14.45 -16.15   **Oral presentations - Exposome, Human Health and biological mechanisms**

(10min presentation + 2min Q/A)

Selected talks

- *The early life physical and social external exposome and child selective attention: a multi-cohort study*. Carmen Peuters and Núria Botella, ISGlobal.

- *Prenatal nut and fish intake and neuropsychological function trajectories from birth to 15 years of age: a population-based cohort study.*   Ariadna Pinar Martí, ISGlobal.

- *Prenatal exposure to mixtures of endocrine-disrupting chemicals in association with obesity in childhood and adolescence*. Nuria Güil-Oumrait, ISGlobal.

- *Early life environmental exposure and childhood morbidity in Southern Mozambique: An exposome approach*. Stefan Sieber, ISGlobal.

- *Placental epigenome-wide association study of in utero exposure to phthalates*. Hana Vespalcova, ISGlobal.

- *Common genetic variants associated with urinary phthalate levels in children: A genome-wide study*. Mariona Bustamante, ISGlobal.

- *Impact of Maternal Dietary Exposure on Plasma Metabolome, Gut Microbiota, and Immunological Development in Rat Offspring During Pregnancy and Breastfeeding*. Rafael Tume Peralta, UB.

16.15-16.30   Guest speaker: Ville Pimenoff - Associate Professor in Oulu University, Finland. *Personalized metagenome monitoring of exposure for pregnant women*.

16.30-16.40   Closing remarks – End of the event

Poster sessions

- *Advanced suspect screening approach to unveil children's personal chemical exposome using silicone wristbands*. Camilla Guerrini, IISPV.

- *Environmental Contaminant Exposure in Children: A Study of Urine Samples*. Julen Segura Abarrategui. CID-CSIC.

- *Quantification of Tire Rubber Additives and Transformation Products in Silicone Bands and Urine: A Focus on Exposure Assessment*. Francesca De Angelis, CID-CSIC.

- *Novel sample treatment strategies for a holistic chemical exposome characterisation through LC-HRMS*. Ruben Gil-Solsona, IDAEA-CSIC.

- *Characterization of human and environmental exposures to Tire Rubber Additives and their Transformation Products*. Mercè Garí, IDAEA-CSIC.

- *Longitudinal cardiometabolic diseases risk prediction: A deep learning approach with LSTM models*. Marina Camacho, UB.

- OnBREATHE: personal air quality monitoring & data digitalization to track chronic respiratory diseases. Dídac Roda Pitarg, IISPV.

- Exploring potential exposure-disease associations through air particulate matter analysis, wastewater based epidemiology, and characterization of brain tumors' chemical exposome. Maria-Christina Nika, IDAEA-CSIC.

- Brain Perfusion Changes from High Ultra-Processed Food Consumption Mediate Depression. Adam Alvarez-Monell, UAB.

- Understanding and preventing the impact of endocrine disruptors in sensitive populations. Chiara Baudracco, Eurecat.

- Exploring the Impact of Air Pollutants and Socioeconomic Factors on Respiratory Cancer Mortality in Italy: Insights from Explainable Machine Learning Models. Donato Romano, University of Bari/ISGlobal.

- Modeling the Initiation of Lung Neuroendocrine Cancers by Directing Environmental Cues in CRISPR engineered Pulmonary Organoids. Andrés Marco Giménez, EMBL.

- The effect of night shift work on microbiome composition. Raquel Galán, ISGlobal.

- Assessment of Dermal Migration of Plastic Additives from Consumer Products. Sandra Callejas-Martos, CID-CSIC.

- A pilot study: developing an ultra-processed diet for rats and future mechanistic investigations. Veronica Palomera-Avalos, UAB.
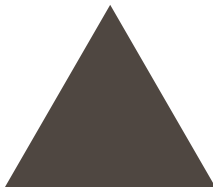
Keynote speakers

Montse Marquès Bueno, Universitat Rovira i Virgili.

Advances in Measuring Environmental Exposures in Biological Samples and Their Epidemiological Implications

The accurate measurement of environmental exposures in biological samples is critical for understanding the complex relationships between environment and health. Environmental exposures have traditionally been measured by means of targeted approaches, which involve the precise quantification of known environmental contaminants in biological samples. Utilizing techniques such as low-resolution mass spectrometry (LRMS), targeted analysis provides high sensitivity and specificity, allowing for the detection of low levels of specific chemicals. In contrast, untargeted methods aim to profile a broad spectrum of unknown and known compounds simultaneously. Techniques such as high-resolution mass spectrometry (HRMS) enable the comprehensive analysis of xenobiotics and metabolites, providing a global snapshot of the chemical exposome. Besides saving time and preserving the amount of biological sample, this approach is particularly useful for hypothesis-generating studies, as it can uncover novel exposure biomarkers and pathways that were not previously considered.

The integration of targeted and untargeted approaches, along with epidemiology, enhances our ability to elucidate the multifaceted interactions between environmental exposures and health outcomes. By combining these methodologies, we can validate novel biomarkers discovered through untargeted screening using targeted quantification, thereby strengthening the causal inference in epidemiological studies.

This keynote talk will introduce and compare the different approaches for measuring the environmental exposures, highlighting the last advancements in LRMS and HRMS, showcase their application in epidemiological research, and provide concrete examples from the research carried out by my group at IDAEA-CSIC. By bridging the gap between environmental exposure assessment and epidemiology, we can better understand and mitigate the health impacts of environmental contaminants.

Biography

Dr. Montse Marquès is an expert in biomonitoring, exposure science, and the investigation of adverse health outcomes. With over 12 years of experience, Dr. Marquès has significantly advanced the understanding of the complex interactions between environmental exposures and human health. She currently holds the position of Ramón y Cajal Fellow at the Institute of Environmental Diagnostic and Water Research within the Spanish National Research Council (IDAEA-CSIC).

Dr. Marquès earned her Ph.D. in Environmental Toxicology and Chemistry from Universitat Rovira i Virgili (Spain), where she developed targeted approaches for measuring pollutants in environmental and biological samples. During her tenure as a Marie Curie postdoctoral researcher, she combined high-resolution mass spectrometry with exposome-wide association studies at Antwerp University (Belgium) and Columbia University (United States). Her current research focuses on combining omics science with novel epidemiological models, with a special emphasis on women's health.

Her research has been widely published in top-tier scientific journals. She is the PI of the INSULIN mother-child cohort from Hospital Joan XXIII (Tarragona). As a dedicated educator and mentor, Dr. Marquès has served as a lecturer in Environmental Toxicology and Food Toxicology at Universitat Rovira i Virgili for the past six years and is committed to training the next generation of scientists in the field. Additionally, she currently serves as an Associate Editor for two scientific journals (Environmental Pollution and Environmental Advances).


Javier Solana Sánchez, Institut Guttmann.

The Barcelona Brain Health Initiative (BBHI) - A Cohort Study to Define and Promote Determinants of Brain Health.

A graduate in Telematics Engineering and a graduate in Telecommunications Engineering, he holds a master's degree in Telemedicine and Bioengineering, and a PhD in Biomedical Engineering. His expertise is focused on research and innovation in the field of neuroscience, with special interest in the application of technology to improve health services.

During his career, Dr. Solana has participated in more than 18 national and European research projects, many of them focused on innovation and entrepreneurship. For example, he has worked on the development of a mobileHealth coaching solution to monitor and promote healthy habits, as well as o design of data management systems to optimise brain resilience and recovery after neurological inju

He joined the Institut Guttmann's Research, Innovation and Teaching Office in 2016 as the technolo and manager of the Barcelona Brain Health Initiative (BBHI), a large-scale longitudinal cohort stud involved more than 6,000 volunteers.
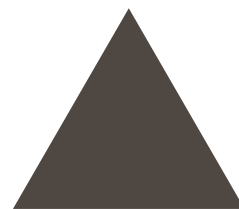
Following the symposium – Event for the General Public

Panel discussion: "Unveiling Hidden Threats: The Impact of Chemical Exposures and Endocrine Disruptors on Public Health"

Brief Description: Join us for a thought-provoking panel discussion as part of the Barcelona Exposome Symposium at the PRBB, open to the general public from 18-19h. This one-hour session will bring together leading researchers from ISGlobal, CSIC and other institutions to explore the invisible but generalized threats posed by chemical exposures and endocrine disruptors. Experts will present how these substances affect our health, disrupt hormonal systems, and what the latest research reveals about minimizing risks. The event aims to raise awareness, encourage dialogue and engage the community in understanding the impact of everyday chemicals on our well-being. Don't miss this opportunity to learn and interact with experts at the forefront of environmental health research!

Day: **September 25, 2024, as part of Researchers' Night 2024**

Time: 18-19h

Location: Centre Civic El Sortidor Plaça del Sortidor, 12, Sants-Montjuïc, 08004 Barcelona

Language: Catalan and Spanish
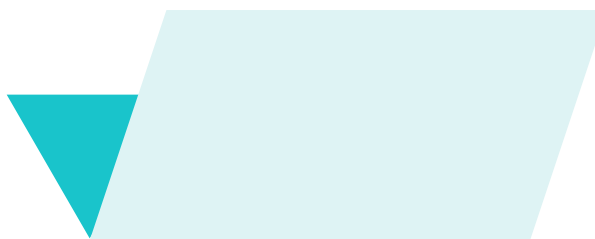
Abstracts

Ana González-Ruiz, IISPV

Evaluating Long-Term Exposure to Endocrine Disruptors: A Comparative Study of Hair, Blood, and Urine Samples

Authors: Ana González-Ruiz, Rodrigo Carneiro, Esteban Restrepo-Montes, Antonio Lobato, Ramón Pujol, Montse Marquès, Rubén Gil-Solsona, Pablo Gago-Ferrero

Endocrine disruptors (EDs) are a group of chemicals frequently found in consumer products that can interfere with the endocrine system, leading to adverse health effects. Traditional assessment using blood and urine samples offers insights into recent exposure but may not accurately reflect long-term exposure due to their relatively short half-lives in the body. Hair, however, integrates exposure over extended periods, providing a comprehensive assessment for biomonitoring studies. In this study, we assessed the presence of EDs in hair samples and compared them with blood and urine samples from a cohort of 10 frontal fibrosing alopecia (FFA) patients and 10 age-matched controls from Hospital del Mar in Barcelona using LC-HRMS (Q-TOF). Among the 48 EDs analyzed, 35 were detected, with the highest number of compounds found in hair samples (63%), followed by urine (42%) and serum (27%). Parabens and flame retardants were consistently present in all matrices and hair samples showed a notably higher concentration range (<LOQ-3134 µg/kg) compared to serum (<LOQ-88.12 µg/L) and urine (<LOQ-26.47 µg/L). The elevated number of compounds detected and the higher concentration range in hair highlight its importance as a biomonitoring matrix for assessing long-term exposure to chemical compounds.

Andrea Unión Caballero, UB

Metabolomic biomarkers for dietary fibre exposure: summary from human studies

Authors: Andrea Unión Caballero, Tomás Meroño, Miriam Martínez-Huelamo, Rikard Landberg, Jytte Halkjær, Gabrielle Riccardi, Giuseppina Costabile, Kia Nøhr Iversen, Sebastian Åberg, and Cristina Andrés-Lacueva

Introduction/Background: Dietary fibre consumption has been linked with improved cardiometabolic health, however, human studies have reported large interindividual variations. Accurate measurement of dietary fibre intake is challenging due to the limitations of dietary questionnaires and individual variability in response. Under this context, metabolomic biomarkers for dietary fibre intake/effect are crucial for identifying individuals with particular host/gut microbiota metabolic characteristics that interact with dietary fibre exposure.

Methods: A targeted-metabolomics analysis was performed in plasma samples from three studies: 1] A one-year observational study with repeated evaluations across 624 participants [DCH-NG MAX study]; 2] A 12-week randomized controlled weight loss trial with 212 participants on either a high fibre rye diet or a refined wheat diet; 3] A 3-week crossover postprandial trial comparing different types of fermentable cereal fibres.

Results: Several plasma metabolites were consistently associated with fibre intake in all three studies. Most of them were gut microbial metabolites belonging to phenolic acids/phenols (of note, 2,6-dihydroxybenzoic acid, 2-aminophenol, sulfated derivatives of gallic, vanillic and caffeic acid], other gut microbial metabolites like indolepropionic and enterolactones, benzoxazinoids and betainized compounds. Most of these metabolites showed negative associations with cardiometabolic risk factors.

Conclusion: These metabolites may represent a novel class of biomarkers to guide future precision nutrition interventions to maximize their health effects, identifying individuals with particular host /gut microbiota metabolic characteristics that interact with dietary fibre exposure.

Daniel Gutiérrez Martín, IDAEA-CSIC

Exploring the Chemical Exposome in Brain Cancer: A Proof of Concept

Authors: Gutiérrez-Martín D., Gil-Solsona R., Nika M.C., Pons-Escoda A., Díez S., Vidal-Sarro N., Bruna J., Dadvand P., Majós C., Gago-Ferrero P.

Glioblastomas are highly diverse and aggressive brain tumors with a challenging prognosis and low survival rates. Their etiology remains poorly understood, with few established risk factors. Environmental exposures have been implicated in their development, but current studies are limited and inconsistent, particularly regarding exogenous organic chemicals. A comprehensive characterization of the chemical exposome associated with these tumors is lacking. In this proof-of-concept study, we examined 33 glioblastoma samples from the Bellvitge Glioma Cohort (BGC), Spain (2005-present), alongside 20 non-tumoral samples, using high-resolution mass spectrometry-based wide-scope target and suspect strategies. We identified 46 exogenous chemicals in the tumor tissue samples, with 31 confirmed using analytical standards. These chemicals included various industrial compounds (e.g., plastic additives, perfluorinated compounds), personal care products, and pharmaceuticals. Our findings introduce new evidence of these chemicals' presence in brain tissue, emphasizing the need for comprehensive evaluations to understand their potential role in tumor pathogenesis.
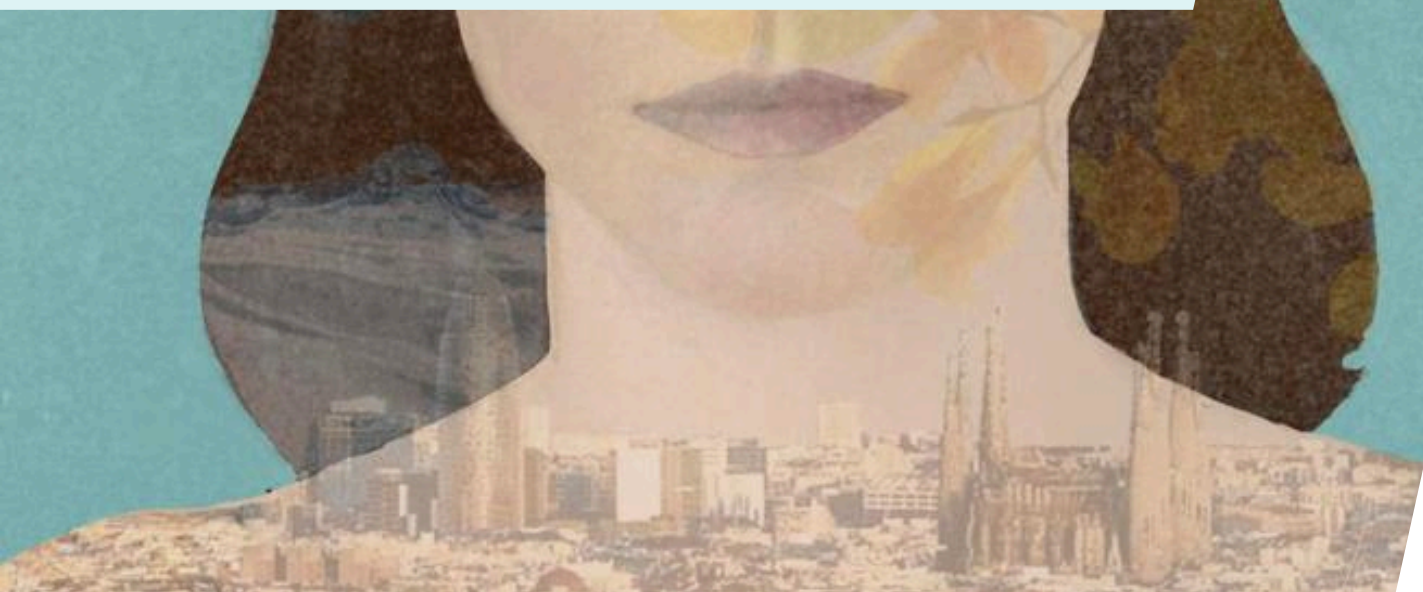
Esteban Restrepo-Montes, CID-CSIC

Assessment of potentially hazardous chemicals during pregnancy

Authors: Restrepo-Montes Esteban; Sunyer-Caldú Adrià; Golovko Oksana; Marzo-Díaz Raquel; Laura Gómez-Roig, Bustamante Mariona; Elisa Llurba, M Dolores Gómez, Rivas Lara Ioar, Dadvand Payam; Sunyer Jordi; Gil-Solsona Ruben and Gago-Ferrero Pablo

Chemical exposures are a major risk factor in the onset of a wide range of chronic diseases, and this risk increases during early stages of gestation, with potential adverse effects throughout the life course. This study aimed to comprehensive evaluate the occurrence of organic contaminants in pregnant women, and their potential transfer to the foetus.To achieve this, we focused on two biological matrices (serum and placenta). The chemical expsome was measured with a validated methodology based on liquid chromatography coupled to high-resolution mass spectrometry that allowed to assess >700 potentially hazardous chemicals in 294 maternal serum (third trimester of pregnancy) and 253 placenta samples (114 nested with serum) from the Barcelona Life Study Cohort (BiSC). For serum and placenta different a wide amount of chemicals were found (149 and 147, respectlively), with 33 and 60 chemicals having a detection rate >50% and at least 28 and 52 >80%. These chemicals included plasticizers, tire additives, UV-filters, PFAS, personal care products, among others. The concentrations found varied, ranging from low ng/L to low mg/L . Sixty-three of the chemicals detected were present in both placenta and serum, for index, tris(2-chloroisopropyl) phosphate, N,N'-Diphenylguanidine and Di-n-octyl phthalate. The concentration ratios between these matrices were studied, revealing significant variability depending on the physicochemical properties of the chemicals, with some showing higher retention in one matrix than the other. Further studies will be conducted, including the analysis of paired cord blood samples, to better understand how the placental barrier affects the mobility of chemicals from maternal to cord blood.

Meryl Cruz, UB

Exposome in Nutrition and Personalized Medicine. Multi-targeted quantitative platform for exposome-based metabolomics

Authors: Miriam Martínez Huélamo, Meryl Cruz, Rommel Alejandro Carballo Castañeda, Anna Guadall Roldán, Montse Rabassa Bonet, Tomás Meroño, Rupasri Mandal, David Wishart, Cristina Andres Lacueva

Introduction: Exposome refers to the totality of exposures from a variety of external and internal sources including chemical and biological agents or radiation, from conception and throughout a lifetime. Taken together, the interactions between these factors throughout life would lead to the development of pathologies or a particular biological ageing trajectory. Our group initiative seeks to fill this knowledge gap by offering a unique opportunity to explore the exposome in granular details.

Methods: A multi-targeted quantitative metabolomic methodology for the study of the Exposome and exposures have been developed and validated.

Results: The coverage of our methodology comprises more than 2000 metabolites including 450 food- and gut microbiota-derived metabolites, 50 common pollutants, 50 drugs, >900 lipids, 103 amino acids, 106 organic acids, 26 biogenic amines, 52 dipeptides, 32 nucleobases and nucleosides, 20 bile acids, 20 ketone and ketoacids, 11 steroids and hormones, 11 indole derivatives, 5 vitamins and other lifestyle habits biomarkers.

Conclusions: Discovering novel biomarkers for early diagnosis, prevention, and personalized therapy, is essential and highly demanded. Our Exposome methodology quantified >2,000 biofluid biomarkers related to general and specific external factors. Starting point to boost precision nutrition and personalized medicine.

Anna Molas and Ana Cerezuela, AFIN-UAB

Pregnant and lactating women facing climate emergency in Barcelona: an anthropological approach to the environment and perinatal health

Authors: Anna Molas and Ana Cerezuela

A growing body of medical literature emphasizes the irreversible consequences of adverse environmental exposure for women during the perinatal stage. For instance, studies have correlated serious pregnancy issues such as preeclampsia, premature births, reproductive losses, and stillbirths with extreme temperatures and environmental pollution. Furthermore, research indicates that exposure to poor environmental conditions may have long-term effects on the health of future generations through epigenetic mechanisms. Despite increasing media, social, and political attention towards climate change, environmental degradation and its potential catastrophic consequences, there is a lack of qualitative studies exploring the experiences and needs of women in this context. This presentation offers an anthropological perspective on environmental and perinatal health by focusing on the experiences of pregnant and lactating women in Barcelona. Through their voices, we demonstrate how the "environment" in the city is a broad concept that encompasses gender, socioeconomic, urban, and even touristic constraints that intersect and cannot be easily separated. Our ethnographic exploration underscores the importance of considering cultural, social, and geographic particularities to design effective healthcare and urban policies.

Nicolás Ayala Aldana, ISGlobal

Impact of fatty acid patterns on adolescent neurocognitive function: Insights from neuropsychological assessments

Authors: Nicolas Ayala-Aldana MSc, Ariadna Pinar-Martí MPH, Marina Ruiz-Rivera MPH, Jordi Julvez PhD

Purpose: Neurocognitive function during adolescence is shaped by a combination of behavioral factors, life experiences, and nutritional intake. Fatty acids (FAs) play a pivotal role in brain development and cognitive function. In this study, we investigated the influence of principal FAs patterns on various neuropsychological outcomes, including working memory and decision-making tasks.

Methods: We performed principal components analysis (PCA) to determine fatty acids (FA) patterns. Multiple linear regression was performed to analyze the association between FA with neuropsychological outcomes: Attentional network test (ANT) and Cup Task Roulette; The Cups Task in Risk Adjustment for Gain (CUPRAG) and Cups Task Risk Adjustment for Loss (CUPRAL). We additionally adjusted the linear regression models for child sex, age, and maternal education.

Results: Principal Components (PC) and ANT outcomes are presented, revealing a positive association between Omega-3 PC3 and 2-back ANT (tertile 3: $\beta\_1= 0.20$, 95% CI=0.05, 0.36, p-value<0.05). Conversely, highlights associations between FA patterns and outcomes, indicating a positive association between Omega-3 PC2 and CUPRAG (tertile 3: $\beta1= 0.52$, 95% CI=0.04, 1.01, p-value<0.05), and a negative association between Omega-6 PC3 and CUPRAL (tertile 3: $\beta\_1= 0.52$, 95% CI=-0.63, -0.09, p-value<0.05).

Conclusion: These findings provide valuable insights into the intricate interplay between FA compositions and cognitive function.

Joan Grimalt, IDAEA-CSIC

Simultaneous determination of neonicotinoid, carbamate/thiocarbamate, triazole, organophosphate and pyrethroid pesticides and their metabolites in urine from general population

Authors: Joan O. Grimalt, Carolina M. Bustamante, Natalia Bravo, Mercè Garí

Purpose: Neurocognitive function during adolescence is shaped by a combination of behavioral factors, life experiences, and nutritional intake. Fatty acids (FAs) play a pivotal role in brain development and cognitive function. In this study, we investigated the influence of principal FAs patterns on various neuropsychological outcomes, including working memory and decision-making tasks.

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Conclusion: These findings provide valuable insights into the intricate interplay between FA compositions and cognitive function.

Mahsa Naghavi Sheikholeslami, IISPV

Advanced analytics in pediatric exposomics: Decoding the chemical exposome through machine learning

Authors: Mahsa Naghavi Sheikholeslami, Camilla Guerrini, Óscar Gómez, Noelia Ramírez

Early-life exposure to environmental chemicals raises chronic disease risks, requiring a thorough understanding of the chemical exposome for effective interventions. Our study improves the characterization of the chemical exposome in children using advanced data analysis, including machine learning and clustering methods. Children (n=218, 8-12 years old) from urban and industrial locations in Tarragona, Spain, wore silicone wristbands (SWBs) for 7 days. SWBs extracts were analyzed using advanced wide-scope suspect screening by high-resolution mass spectrometry with liquid and gas chromatography. Machine learning algorithms classified exposure profiles and identified critical chemical exposures against socioeconomic characteristics and children's behaviors. Clustering algorithms deciphered hidden patterns in exposure profiles, revealing significant differences in chemical exposure and sociodemographic factors between groups. For example, children's exposure to tobacco-specific toxicants was higher in disadvantaged areas and homes, while children with stable families, and higher-educated parents exhibited lower exposure levels. This study demonstrates the utility of data analysis techniques in revealing complex relationships within the chemical exposome, providing critical insights into the impact of environmental exposures on children's health. These findings highlight the importance of integrating analytical techniques and machine learning in exposomics studies to inform comprehensive health protection strategies.

Sofía Aguilar Lacasaña, ISGlobal

Green space exposure and blood DNA methylation at birth and in childhood – A multi-cohort study

Authors: Sofia Aguilar-Lacasaña*, Irene Fontes Marques*, Montserrat de Castro, Payam Dadvand, Xavier Escribà, Serena Fossati, Juan R González, Mark Nieuwenhuijsen, Rossella Alfano, Isabella Annesi-Maesano, Sonia Brescianini, Kimberley Burrows, Lucinda Calas, Ahmed Elhakeem, Barbara Heude, Amy Hough, Elena Isaevska, Vincent W V Jaddoe, Deborah A Lawlor, Genevieve Monaghan, Tim Nawrot, Michelle Plusquin, Lorenzo Richiardi, Aidan Watmuff, Tiffany C. Yang, Martine Vrijheid**, Janine F Felix**, Mariona Bustamante**
*Shared first authors **Shared last authors

Green space exposure has been associated with improved health outcomes. However, the biological mechanisms remain unclear. This study aimed to explore the association between green space exposure and DNA methylation in cord and child blood. Data from eight European birth cohorts, including 2,988 newborns and 1,849 children, were analysed. Two indicators of green space exposure were assessed: surrounding greenness using Normalized Difference Vegetation Index (NDVI) within 100m and 300m buffers and proximity to green space (having a green space $\geqslant$ 5,000m² within 300m).

These indicators were evaluated during pregnancy and cumulatively from pregnancy to the time of DNA methylation assessment. DNA methylation was measured using Illumina 450K or EPIC arrays. Robust linear regression models were fitted to identify differentially methylated positions (DMPs), and cohort results were meta-analyzed using fixed-effect inverse variance weighted methods. Differentially methylated regions (DMRs) were identified with Enmix-combp and DMRcate methods.

There was no statistical evidence of pregnancy or cumulative exposures associating with any DMP. However, surrounding greenness was inversely associated with four DMRs in ADAMTS2, KCNQ1DN, SLC6A12, and SDK1 genes. DNA methylation of two of these genes have been previously reported in relation to green spaces. Overall, we found little evidence of the association between green space exposure and blood DNA methylation.

Laura Sistach, Eurecat

HYPIEND Digital Tool: A Personalised Platform for Reducing EDC exposure

Authors: Laura Sistach and Silvia Orte

Endocrine-disrupting chemicals (EDCs) pose significant health risks, especially interfering with the endocrine system's development and function. While guidelines exist, they are not tailored to individual needs nor designed in an engaging format. The HYPIEND Digital Tool (HDT) provides personalised guidance on lifestyle modifications, empowering individuals to make informed choices by significantly reducing EDC exposure and its associated risks through digital innovation combined with behavioural science. Through engaging educational content and interactive tools tailored to users' unique characteristics, HDT users can identify and prioritise behaviours for change. HDT helps users understand the significance of various lifestyle categories (e.g. food choices) and select specific behaviours to focus on (e.g. avoiding canned food and drinks). Each target behaviour includes missions—small challenges and tasks designed for user engagement. The platform fosters community building, allowing users to connect, share experiences, and support each other in reducing EDC exposure. Two clinical studies will be conducted across three European countries involving pregnant women from pregnancy to the infant's age of 18 months and prepubertal children through a three-year primary school intervention. Both studies will enable direct comparisons to detect a decrease in EDC concentrations in the intervention groups compared to control groups.

Carmen Peuters and Núria Botella, ISGlobal

The early life physical and social external exposome and child selective attention: a multi-cohort study

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Objective: The physical and environmental surrounding (e.g., air pollution) and social factors (e.g., family affluence) during early life may influence selective attention but have mainly been investigated in isolation. We aimed for a comprehensive approach to identify the most important physical and social predictors of selective attention in children. Methods: Selective attention was measured using computerized tests in children aged 5-16y from five studies across Europe (N=11,738). Individual-level exposures were assessed by questionnaires, area-level (child's residence) exposures by public databases, remote-sensing data, and modelling approaches. Two exposure periods were considered: (i) conception to 3y old, (ii) 3y old to date at testing. Random forest analyses were performed separately for each study, including op to 46 physical/environmental and 28 social indicators, depending on availability. The single-study results were combined in an adjusted meta-analysis to obtain the order of exposure importance. Preliminary results: From conception to 3y, area-level income, population density, street network, father's occupation, air pollution, green and blue space, area-level household structure, noise, youth/old-age ratio, land use, and migration ranked highest in importance. Results were similar for the 3+y period, but air and noise pollution no longer ranked in the top 15, and father's country of birth, youth ratio, and moving home ranked higher. Conclusion: Indicators from the physical (urban environment) and social (neighbourhood and family socio-economic) exposome rank similar in importance for their association with selective attention. Air and noise pollution rank higher in the first years of life, whereas more social exposures rank higher in later years. Keywords: child cognitive development, selective attention, external environment, exposome, machine learning.

Ariadna Pinar Martí, ISGlobal

Prenatal nut and fish intake and neuropsychological function trajectories from birth to 15 years of age: a population-based cohort study

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Understanding maternal nutrition's role in early brain development is critical, as pregnancy is a period of significant growth for the developing brain. This study assessed the long-term impact of maternal fish and nuts consumption during the first trimester of pregnancy on neuropsychological function in offspring up to 15 years old and examined whether omega-3 fatty acids mediate this association. Conducted within the INMA Project, this multicenter, population-based cohort study followed 2506 women from pregnancy, with final analyses including 857-1737 children. Maternal nut and fish intake was assessed using a validated food frequency questionnaire. Children's neuropsychological functions were evaluated using standardized tests for attention, working memory, and fluid intelligence. To assess the effect trajectories, linear mixed-effects models were used, and a mediation analysis was performed to estimate the proportion of the effect that was mediated by omega-3s (sum of EPA, DHA and ALA), measured in cord blood at the time of delivery. Higher maternal nut consumption was associated with better attention function, working memory, and fluid intelligence. Similarly, higher maternal large fatty fish consumption was linked to improved attention and fluid intelligence. Omega-3 fatty acids mediated the positive effects on attention function, explaining 8-14% of the total effect. These results emphasize the importance of maternal diet during pregnancy, particularly the intake of nuts and large fatty fish, in fostering optimal cognitive development in offspring.

Nuria Güil-Oumrait, ISGlobal

Prenatal exposure to mixtures of endocrine-disrupting chemicals in association with obesity in childhood and adolescence

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Background: Prenatal exposure to endocrine-disrupting chemicals (EDCs) may contribute to childhood obesity, but few studies have tracked these associations into adolescence while assessing EDC mixtures, toxicological interactions, and protein pathway mediation.

Methods: We examined 1301 mother-child pairs from the Human Early Life Exposome (HELIX) project across six European countries. We analyzed 45 chemicals from nine EDC classes measured in urine and/or blood collected during pregnancy. BMI WHO z-scores were calculated for childhood (6-12 years; N=1301) and adolescence (13-18 years; N=607). We used penalized multi-group Bayesian Weighted Quantile Sum Regression (BWQSR) to assess EDC mixture associations with overweight in childhood and adolescence, and signed-iterated Random Forest (SiRF) to search for synergistic interactions. Protein mediation pathways were identified in the relationship between prenatal chemical mixtures and BMI z-score in adolescence.

Results and Conclusion: Adjusted multi-group BWQSR indicated , in both childhood and adolescence periods, higher exposures to the metal mixture (OR [95%CrI] per quartile mixture increase = 1.47 [1.10, 1.98] and (1.10 [0.66, 1.79], respectively), and the organochlorine pesticide mixture (OR [95%CrI] = 1.48 [1.23, 1.79] and 1.46 [1.11, 1.97], respectively) were associated with higher odds for being overweight. BWQSR-SiRF found synergistic interactions in childhood (cadmium with PBDE-47 and DDE) and adolescence (cadmium with manganese and butyl paraben) in subsets of the population with higher concentrations. Mediation analysis suggested pathways like JAK-STAT and NF-kappa beta mediated the association between prenatal metal exposure and increased BMI z-score in adolescence (57% and 65%, respectively).

Stefan Sieber, ISGlobal

Early life environmental exposure and childhood morbidity in Southern Mozambique: An exposome approach

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Introduction: We aimed to quantify the association between the early life external exposome and hospital visits among children under 5 years in a semi-rural area of Southern Mozambique.

Methods: We used data on 19,661 children aged 0-5y born in the Manhiça district. We used 28 exposures covering four external exposome domains: socioeconomic adversity, family instability, household environment, surrounding residential environment. We conducted domain-specific Multiple Correspondence Analysis and Principal Component Analysis to reduce dimensionality and derive interpretable components representing each domain. We selected dimensions/principal components (PCs) that explained at least 80% of the variance. Dimensions/PCs were used as linear variables in adjusted negative binomial regression models to estimate the association between each external exposome domain and the number of hospital visits.

Results: The strongest effects were found in the surrounding residential environment and socioeconomic adversity domains, while the household environment was not significant after adjusting for other domains of the external exposome. The family instability domain was not associated with the number of hospital visits, even before adjusting for other domains.

Discussion: Results highlight the importance of comprehensive characterization of the diverse external exposome domains of children in a low-income context and their association with morbidity.

Hana Vespalcova, ISGlobal

Placental epigenome-wide association study of in utero exposure to phthalates

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Phthalates, plasticizers present in everyday consumer and food products, are well-known endocrine-disrupting chemicals. Fetal development is a highly vulnerable period to environmental stressors with long-term health effects, and the placenta plays a key role in this process. Our aim was to investigate epigenetic changes in placenta associated with in utero phthalate exposure. The study was conducted in a population of 469 women-child pairs from the Barcelona Life Study Cohort (BiSC) with information on concentration of 14 phthalates measured in pools of 10-12 maternal urine samples collected at 12 (n=349) and 32 (n=404) weeks of pregnancy, and on placental DNA methylation assessed at birth with the EPIC array. We applied robust linear regressions adjusted for covariates to examine the association between phthalate exposure and DNA methylation in CpG sites, and conducted functional enrichment analysis for the biological interpretation. After multiple-testing correction, we observed 6 statistically significant CpGs associated with the whole pregnancy concentrations of 6 phthalates. When analysing the two trimesters separately, effect sizes of main results were slightly decreased, and additional 25 CpGs were identified, mostly with levels at 12th week. Genes associated with these CpGs are involved in endocrine, immune, and neurological pathways. Our results contribute to understanding the molecular mechanisms associated with in utero exposure to phthalates and its impact to placental and fetal health.

Mariona Bustamante, ISGlobal

Common genetic variants associated with urinary phthalate levels in children: A genome-wide study

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Introduction: Phthalates are plasticizers in consumer and industrial products that act as endocrine disruptors and are linked to several diseases. We performed genome-wide association analyses (GWAS) to identify Single Nucleotide Polymorphisms (SNPs) and Copy Number Variants (CNVs) influencing phthalate metabolism and associating with differences in urinary phthalate levels.

Methods: We studied 1,044 European children from the HELIX cohort, measuring urinary levels of 10 phthalate metabolites via liquid chromatography coupled to mass spectrometry. SNPs were genotyped with the Infinium GSA and imputed with the HRC panel. CNV consensus regions were identified with PennCNV and CNVRanger. GWAS of SNPs and CNVs were conducted using PLINK and SNPassoc for the 10 phthalates and 6 phthalate ratios. Functional annotation of suggestive SNPs was performed with the FUMA web-tool.

Results: We identified four genome-wide significant loci at FECHP1 gene for oxo-MiNP_oh-MiNP ratio, at SLC17A1 for MECPP_MEHHP ratio, at RAPGEF1 for MBzP concentration, and at CYP2C9 for MECPP_MEHHP ratio. Two CNVs overlapping MRGPRX1 for oh-MiNP and SLC35F2 for MEP were also identified. Functional annotation pointed to genes involved in detoxification phases I and II, molecular transfer across membranes, and renal excretion.

Conclusion: Genome-wide genetic screenings identified 2 known and 4 novel loci implicated in phthalate metabolism.

Rafael Tume Peralta, UB

Impact of Maternal Dietary Exposure on Plasma Metabolome, Gut Microbiota, and Immunological Development in Rat Offspring During Pregnancy and Breastfeeding

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Introduction: The benefits of the mother's dietary exposure during breastfeeding for the offspring's immunological development remain underexplored. We aimed to study the impact of a healthy diet during gestation and lactation on plasma metabolome and gut microbiota of dams and pups, and their relationship with immunological markers.

Methods: Female Lewis rats were fed during gestation and lactation: a) healthy diet, with soy protein, inulin, and fish oil; b) unhealthy diet, enriched in saturated fat and animal protein; or c) standard diet. Dams and two pups/litter were sacrificed at weaning (day-21). Metabolites in all 45 samples were measured using a targeted exposome-based UPLC-MS/MS metabolomics method. Associations with cecal microbiota (16S rRNA sequencing) and immunoglobulins (Luminex) were assessed through linear mixed models, and further explored via Multiple Factor Analysis.

Results: The separation by diet of the pups was characterized by changes in the mother's metabolome and gut microbiota. Maternal and offspring metabolomes were closely related (R2=0.63). In pups, eleven metabolites and three bacteria genera, showed a positive association with immunological markers.

Conclusions: Exposure to a healthy diet during gestation and lactation induced major changes in metabolites and, to a minor extent, in gut bacteria. These changes were associated with pup's immune system, highlighting the importance of maternal dietary exposure.

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