

ANALYTICAL PLATFORM FOR EXPOSOME RESEARCH

DESCRIPTION OF THE TECHNOLOGY

The risk of chronic disease is attributed to both genetic and environmental factors. For most of the diseases with the greatest contribution to mortality in developed countries, non-genetic (environmental) factors are attributed a risk of 70-90%, although the specific etiological factor is not defined. It is therefore essential, if we want to advance in the discovery of the main causes of chronic diseases, to adopt a more balanced and holistic approach, in which, together with genetic research, the characterisation of "environmental exposure" is integrated, from a comprehensive and quantitative perspective, researching all areas of the environment that can contribute to the development of chronic diseases. The genome needs to be completed with the exposome.

The term Exposome refers to the totality of environmental exposure at all stages of life, and it has been pointed out that it undoubtedly plays a primary role in the development of chronic diseases. The ultimate purpose of Exposome research is the identification of risk factors in epidemiological studies.

In this context, Human Biomonitoring (HBM) is an effective tool for understanding the magnitude of human exposure from all sources and routes of exposure, through which the biomarkers of exposure are determined: stressors (parent compounds) or their metabolites, identified in different biological fluids such as blood, urine, hair, breast milk, etc.

A recent report by the Lancet Commission (Landrigan et al. 2018) concludes that pollution is the main cause of chronic diseases, and points out that the current estimate of the burden of disease attributable to it may be only the tip of the iceberg. Many of these pollutants are not yet well quantified or characterised in relation to their health effects. Therefore, data corresponding to internal exposure are necessary to unravel the exposure and derive associations between Exposome and disease. In this area, exposure to mixtures of chemical substances is of significant importance.

Exposome analysis is fundamentally based on the high capacity of the most advanced high-resolution mass spectrometry (HRMS) equipment. Compared to other analytical techniques, Mass Spectrometry (MS) has the advantages of high sensitivity, selectivity and the ability to identify unknown metabolites chemically. When combined with chromatography it allows the detection of thousands of compounds in a global sample analysis. High resolution and exact mass spectrometry (HRMS) instruments, such as the time of flight detector (TOF) the Orbitrap, operating in full scan, are the most widely used analytical platforms. These instruments provide the possibility to perform target analysis or post-target screening of suspicious substances, as well as non-target analysis. In the non-target analysis the analytical signals (raw data)

conveniently treated, allow to compare the "exposome" (for example in urine) between the cases (exposed) and the controls (in case of an epidemiological study), and consequently to elucidate those compounds that can have relevance or be associated with the studied disease. The screening of suspects requires the development of databases (500-1000 substances) that include data such as the exact mass, the type of ionization and fragments, suspicious biomarkers, and conduct targeted searches in raw data without the need for reference standards.

The technological equipment will include:

1. A high-resolution, dual-focus mass spectrometry system (HRGC-HRMS). This system is the reference instrumentation for the confirmatory analysis of dioxins and in turn allows the analysis of persistent and/or emerging organic pollutants and includes:
 - One magnetic sector mass spectrometer with high resolution and double focus.
 - Two gas chromatographs connected to the mass spectrometer.
2. A liquid chromatography system coupled to a high resolution Orbitrap mass spectrometer (Q EXACTIVE HF ORBITRAP LC-MS/MS).
3. A liquid chromatography system coupled to an ionic mobility system and a QTOF spectrometer (VION IMS QTOF).

The equipment of the Platform is located in the facilities of the Public Health Laboratory of Valencia (LSPV) of the Directorate General of Public Health.

The research carried out by FISABIO in the context of Biomonitoring and the Exposoma study has been developed in the context of different projects such as Developmental neurotoxicity assessment of mixtures in children, the FP7 Program of the EU, the BETTERMILK project (focused on contaminants in human milk) in collaboration with the research institute La Fe; the BIOVAL Program, which is the Biomonitoring tool used by the General Directorate of Public Health to evaluate the exposure of Valencians to food contaminants and the H2020 Project, Human Biomonitoring for Europe (HBM4EU), in which the exposure of European citizens to different pollutants, while giving scientific support to chemical safety and health protection policies.

The combination of the previous knowledge of FISABIO's CASA group and the availability of technological infrastructures allow us to offer the methodology developed for biological monitoring (urine, blood, hair, serum...) of environmental contaminants as well as for the study of the Exposome.

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MARKET APPLICATION SECTORS

The scientific equipment available can give support to projects in the field of biological monitoring of environmental pollutants (including emerging) and the study of the Exposome, and constitute as a support platform for those research centres that require it.

TECHNICAL ADVANTAGES AND BUSINESS BENEFITS

The advantages of this platform are:

- 1) It provides a powerful analytical support to the set of research related to the EXPOSOMA research
- 2) It enables the development of studies that provide better evidence on the exposure of the population to chemical substances (and their mixtures) and their influence on health (causes of chronic diseases)
- 3) It allows a full integration in the European Human Biomonitoring Platform (HBM4EU).
- 4) Establish bridges between research and public health policies, so as to increase the benefits for society in terms of improving food and environmental security.

INTELLECTUAL PROPERTY RIGHTS

The equipment and knowledge of the research group allows the integral approach of projects that contemplate the biological monitoring of environmental pollutants such as the study of the Exposome, both from its conception through consulting and technical/scientific support, as during its performance, completion and publication.

The acquisition of the HRGC-HRMS system has been financed by the Comunitat Valenciana 2014-2020 ERDF funds.

COLLABORATION SOUGHT

Collaboration with other research groups and projects, national and international, in the field of human biomonitoring of environmental pollutants and/or the Exposome study.

RELATED IMAGES



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