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Newsletter

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EDITORIAL

This second EXPOsOMICS newsletter marks the third year of the project and takes stock of both the progress achieved and the challenges that remain.

There have been many exciting new developments since our last newsletter. One of them is the extension of the EXPOsOMICS project with two new teams:
Dr Tim Nawrot from EnvironAge is joining the EXPOsOMICS family, bringing a large new cohort of children to the project and coordinating the children's cohort across Europe.
In Italy, Dr Alessio Naccarati and Dr Sabrina Bertinetti from the Human Genetics Foundation in Turin are joining forces and are coordinating a new leg of the project to measure environment pollutants in Turin with 40 volunteers, each equipped with a personal exposure monitoring (PEM) backpack. We take this opportunity to warmly welcome them on board.

In this second newsletter, we give an overview of the various projects involved in EXPOsOMICS. Dr Augustin Scalbert puts metabolomics in the context of EXPOsOMICS, and Dr Laia Font-Ribera provides insight into the second step of the PISCINA project.
This newsletter also provides information on workshops, important publications related to the project, and upcoming events.

Veronique Terrasse
IARC

Updates: In a nutshell

On 2 and 3 October 2014, members of the project met at CREAL, Barcelona for the Third Annual Meeting to share updates on their respective projects.

The PEM campaigns have been completed in Basel and Turin (including third rounds) and are almost complete in Norwich, INMA (Spain), and the Netherlands (second round).

Samples from PISCINA, Tapas2, MCC, Oxford Street, and Turin and Basel PEM have been sent to the laboratories, and the transcriptomics and metabolomics analyses for Piscina and Tapas2 have been completed.

EnvironAge is now coordinating the children's cohort, and the phase 2 analysis of the cohort has started, such as the ALSPAC analyses.

Air Pollution Exposure Assessment: Exposure measurements in Oxford Street and Hyde Park have been completed, as well as the Tapas2 study.

Interview with Dr Augustin Scalbert

Metabolomics and the Exposome

Dr Augustin Scalbert is in charge of implementing the metabolomic analyses of the biosamples collected in the EXPOsOMICS project. Based in Lyon at the International Agency for Research on Cancer (IARC), Dr Scalbert is also part of the Biomarkers Group in IARC's Section of Nutrition and Metabolism. In this interview, Dr Scalbert describes how metabolomics is a useful new tool to help measure the exposures experienced by an individual during the life-course.

Why use metabolomics to measure the exposome?

We are exposed to a considerable number of chemicals that are part of our environment. Many of these chemicals, derived from our diet, the air we breathe, the water we drink, or from consumer goods we commonly use, may influence biochemical and physiological functions in our body and affect our health.

A number of these chemicals are today well characterized and may be monitored to mitigate exposures and toxic effects. Some are also used as surrogate biomarkers for assessing exposure to various environmental, dietary, or lifestyle factors that cannot be easily and reliably measured through classical approaches, often based on the use of questionnaires.

On the other hand, many other chemicals may also be responsible for part of the disease burden that is still unexplained today. Their nature remains largely elusive, and this is why there is much interest in developing new tools to measure the exposome in a more comprehensive way and in implementing these tools in large-scale epidemiological studies to identify exposures most strongly associated with disease risk.

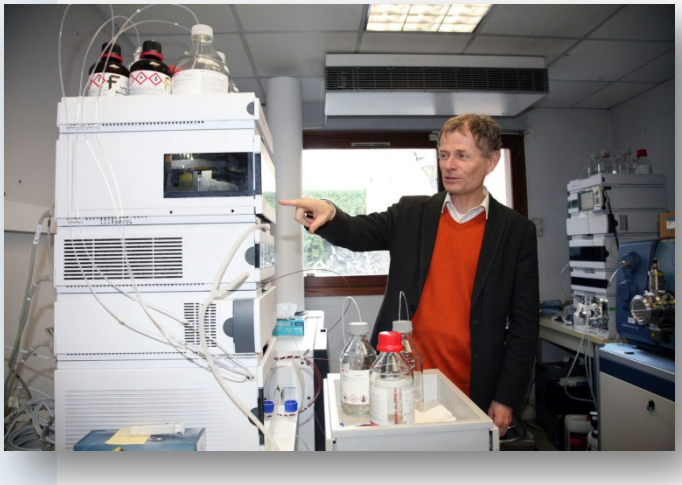
Metabolomics is one of these tools; what does it consist of?

Metabolomics combines powerful analytical techniques with multivariate statistics and bioinformatics to identify in blood, urine, and other biospecimens, in a fully agnostic way, compounds/metabolites that are associated with particular lifestyle or health conditions. Much progress has been made in analytical techniques, and modern mass spectrometers today enable the measurement of hundreds to thousands of low-molecular-weight compounds present in biospecimens like blood or urine.

Interview with Dr Augustin Scalbert

Concretely, how do you implement metabolomics in the EXPOsOMICS project?

As part of the EXPOsOMICS project, we implement metabolomic approaches in well-designed intervention and cohort studies to identify new biomarkers of exposure to air pollution or water contamination. A high-resolution time-of-flight mass spectrometer is used to measure the exposome in blood samples. Large data sets consisting of more than 14 000 signals per sample, corresponding to several thousand metabolites, have been acquired to compare individuals exposed and non-exposed to air pollution (Oxford Street, RAPTES, and TAPAS studies) or water disinfection by-products (PISCINA study). Signals characteristic of the exposed groups are now being identified. Some of these signals are derived directly from chemicals to which individuals have been exposed. To facilitate their identification, we have developed the Exposome-Explorer database, in which all information on established or putative biomarkers measured in various populations exposed to air pollution or water contaminants has been collected from the scientific literature. In addition, other signals characteristic of the exposed groups could also correspond to endogenous metabolites over- or under-expressed, as a consequence of the exposures. Their identification and their integration with other omics data could shed new light on the metabolic and biological effects resulting from these exposures.



Has this approach been used in the past in similar research?

Similar agnostic metabolomic approaches have been successfully used to identify novel dietary biomarkers or to reveal metabolic changes associated with diseases or with intermediate end-points for diseases. Much less is known about environmental exposures such as air pollution and water contamination. This is precisely one of the goals of the EXPOsOMICS project, to see:

(i) if such an agnostic approach is sensitive enough to reveal new biomarkers for these exposures, (ii) if these biomarkers effectively replicate in different intervention studies, and (iii) if they can be validated in populations showing varying levels of exposures. EXPOsOMICS, with unique personal exposure data collected in well-controlled intervention studies or observation studies, offers an ideal setting to address these questions.

Interview with Dr Laia Font-Ribera

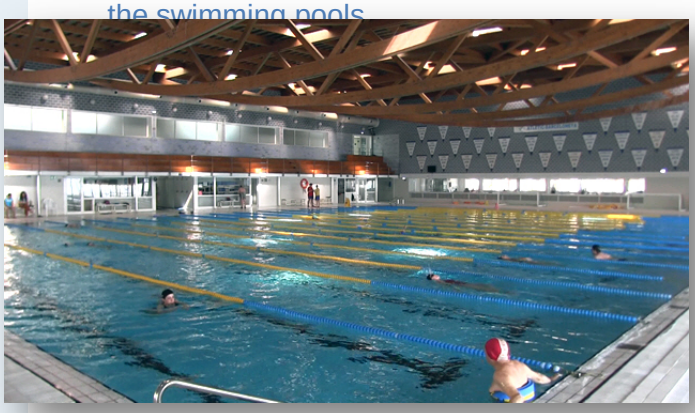
Based in Barcelona, the Centre for Research in Environmental Epidemiology (CREAL) runs the epidemiological study PISCINA, which evaluates potential risks linked to chemicals and disinfection by-products used in swimming pools.
The first part of the PISCINA project has been finalized, and Dr Laia Font-Ribera, who is coordinating the project at CREAL, gives an update on the state of advancement of Piscina2.

Could you please give us an update on the project?

We ended the field work at the end of 2013. We finished working with all the volunteers and with the collection of samples. All the samples have been sent to the laboratories and we have received results for almost all of them, especially for the exposure assessment part.
The laboratories that are analysing the omics samples are starting to get some results, but we will need to wait quite some time before we can compare the omics with the exposures for which we already have some data.

What can you tell us about those primary results?

A previous study was done five years ago, and if we compare the levels of the disinfection by-products present in the swimming pool water with our recent results, we notice that the levels of trihalomethanes have been reduced. Especially the brominated ones, which are the most toxic trihalomethanes found in water.
In the Barcelona area, we used to find very high levels of these compounds in tap water; therefore, a public health action was undertaken in order to be in line with the law, and eventually the levels have been reduced both in the tap water and in the swimming pools.



So this is good news for the swimmers, right?

Yes, the quality of the water is now much better.

Are there any specific challenges that you are experiencing when analysing the results?

The previous study was done with 50 swimmers, but this time we had a larger group of participants.

Interview with Dr Laia Font-Ribera

A bigger sample was necessary in order to get more reliable results. Some changes in respiratory or genotoxicity biomarkers that were detected in the previous study have not been detected this time. These are only preliminary results, and a possible explanation for this could be due to the fact that the levels of toxicants found in water are now lower.
However, we are in a very early stage of the analysis and we would like to combine the results of the previous studies with those of the recent one. That way we would have a higher range of exposures and this would enable us to see whether in fact when the exposure is low the toxic effects cannot be detected and when the exposure is higher those effects are detected. But we will learn more in the coming months.

What is the next step?
I would say that the next step is to improve the statistical analysis and to wait for the omics results in order to see whether omics can help us understand the mechanisms behind the toxicity.

What could be done to reduce the toxicity?
What we are doing now is analysing the biomarkers on the volunteers just after swimming, but we are not certain that this is the best time to collect samples. It is not because we cannot find anything that there are no toxic effects. It is, however, important to reduce the levels of the toxicants both in the water and in the air. So to reduce the levels of toxicants in the air one could, for example, ensure good ventilation of indoor swimming pools.

Some of those toxic compounds (disinfection by-products) are found in tap water, but others are formed within the swimming pool. Those compounds are formed by the reaction of chlorine with organic matter present in the swimming pool, which is brought by the swimmers. By showering just before getting into the swimming pool we bring less organic matter and therefore less toxic compounds will be formed in the water. This is a way of reducing the levels of toxic compounds in the swimming pool.

VIDEO

Exposure Monitoring in Swimming pools

Click PLAY to watch the video

LATEST NEWS

Seminars and Workshops

Investigator's Seminar: On Wednesday 26 November 2014, MRC-PHE Centre held a new Investigator's Seminar at Imperial College London. Research focused on the exposome in practice and was led by Dr Paolo Vineis and Dr Frank Kelly, researchers from Imperial College London and King's College London (information available on website).

Exposomics short course: On Monday 8 December 2014, Imperial College London ran a short course on "Exposomics, Stat XP, Statistical approaches to characterize the exposome from OMICs platforms - overview and perspective", presented by Dr Marc Hyam-Chadeau (information available on website).

Publications

The latest project-related publications can be found on the project website: www.exposomicsproject.eu

In February 2014, *The Lancet* published "Global cancer patterns: causes and prevention". The article focuses on primary prevention as a particularly effective way to fight cancer.

In March 2014, *Environmental Health Perspectives* published "The blood exposome and its role in discovering causes of disease". The article looks at unexplained disease risks and the exposome.

Also in March 2014, *Environmental Research* published "The environmental roots of non-communicable diseases (NCDs) and the epigenetic impacts of globalization". The article looks at how environmental factors (including social adversity, diet, lack of physical activity, and pollution) can become "embedded" in the biology of humans.

In May, *Environmental Health Perspectives* published "Long-term exposure to ambient air pollution and incidence of cerebrovascular events: results from 11 European cohorts within the ESCAPE Project". The study assessed the association between long-term exposure to multiple air pollutants and the incidence of stroke in European cohorts.

On 2 and 3 October 2014, members of the project met at CREAL, Barcelona for the Third Annual Meeting to share updates on their respective projects.

UPCOMING EVENTS

✓ **EC mid-project review for the two projects – Exposomics and HELIX**. This will be held at CREAL in Barcelona, 19-20 May 2015.

✓ The short course **Molecular Epidemiology of Chronic Disease and the Exposome** will be held in Utrecht on 23-27 March 2015. http://www.iras.uu.nl/education/iras_courses_mec2015.php