

Horizon 2020 - H2020-MSCA-ITN-2017



Project: 766251– NEUROSOME

Full project title:

EXPLORING THE NEUROLOGICAL EXPOSOME

D3.1 Application and selection process – overall recruitment

WP3: Recruitment and career enhancement

Lead beneficiary: IUSS

Date: December 2018

Nature: ADM

Dissemination level: Public



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1 Introduction


The current report summarizes the recruitment strategy that has been followed by the beneficiaries of NEUROSOME ITN and presents statistics on the distribution of the candidates during the selection phase.

The NEUROSOME network brings together 9 International Institutions and 5 Partners Organizations and supports the recruitment of fourteen Early-Stage Researchers (ESRs). The research is focused on the development of an integrative biology-based framework starting from human biomonitoring data to unravel causal associations among the genetic predisposition, cumulative exposure to multiple environmental chemicals and neurological disorders. The final aim is to improve scientific knowledge on cause and effect relations between environmental stressors and neurodevelopmental disorders taking into account exposure and health effect modification due to intrinsic (e.g. genetic susceptibility) and extrinsic (e.g. diet and socioeconomic status) factors.

The NEUROSOME project aims to recruit the best possible ESRs, since the ability to attract and recruit the right skills is crucial for the success of the NEUROSOME project. In the recruitment process we have looked for excellent open-minded and team-spirited ESR candidates that show the capacity and enthusiasm to undertake the unique international, interdisciplinary and inter-sectoral training in scientific and transferable skills that is offered in the NEUROSOME project. In order to achieve a successful recruitment we have based the recruitment principles main characteristics on a broad advertisement, nationally and internationally, through various channels available to the members of the consortium to get as many qualified applicants as possible.

In summary, eight (out of fourteen) ESRs were recruited between October and December 2018 and three more were recruited by 1 January 2019. The remaining three candidates have been recruited between February and March 2019 mainly due to the status of visas to be issued. In total five of the selected fellows needed visas to be recruited.

The delays in the recruitment of up to 10 months for three ESRs are not critical and will not impede with the future course of the project. The periods for secondment of the ESRs are flexible and will be adapted according to each recruited fellow's career development plan. Also the training activities, that have purposely been kept flexible, have been adapted to the delays in the recruitment.

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2 Advertisement of ESR positions

In order to ensure that we are selecting from a large, international reservoir of high-quality candidates, and to achieve uniformly high selection standards, we advertised the positions widely but tried to select the ESRs in a small time window. We advertised their positions through the following internationally visible online portals and mailing lists:

- EURAXESS (<https://euraxess.ec.europa.eu/my>)
- NEUROSOME web site (<http://www.neurosome.eu/>)
- Web sites of Beneficiary Organizations
- European projects web sites related to the fields of the exposome
- Job portals (some partners)
- Research communities and mailing lists.

Additionally, the partners used local channels for announcing the ESR positions.


2.1 Eligibility criteria

All applications were required to meet the following eligibility criteria:

- Candidates must have a relevant university degree (master's degree or equivalent) in biomedical/bioinformatics sciences or biological sciences, life sciences or environmental/engineering science or related fields.
- Candidates must have excellent proficiency of the English language.
- Only applications that are complete, in English and in the right order, have been named as needed (SURNAME.pdf; avoid special characters) and that have been submitted by the deadline can be considered eligible.
- The positions are open to all nationalities. However, ESR application has to comply with the European **Commission's Mobility Rules**, meaning that at the time of recruitment candidates must not have resided or carried out your main activity (work, studies, etc.) in the country of the host Organisation for more than 12 months in the 3 years immediately before the start of the employment contract. Compulsory national service and/or short stays such as holidays are not taken into account (European Commission's Guide for Applicants, p. 16).
- Candidates are **an Early-Stage Researcher (ESR) if they** are in the first four years (full-time equivalent research experience) of their research career at the time of recruitment by the host Organisation and have not been awarded a doctoral degree. Full-time equivalent research experience is measured from the date when candidates obtained the degree entitling to embark on a doctorate, even if a doctorate was never started or envisaged. Part-time research experience will be counted pro-rata (European Commission's Guide for Applicants, p. 16).

2.2 Process of recruitment

The recruitment process has followed the rules of the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers (COM (2005) 576 of 11/3/2005), the guidelines of the

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European Charter for Researchers (<http://ec.europa.eu/euraxess>) and the recruitment strategy and rules set in the Marie Skłodowska-Curie participation rules with regard to researcher eligibility and mobility conditions.

The recruitment process was decentralized in order to leave as much freedom to operate as possible to the project partners, when recruiting their ESRs. Therefore, beneficiaries selected their ESRs independently following the rules for MSCA fellows and the rules according to their respective institutions and national/regional requirements. The recruitment process was nevertheless coordinated insofar as a common course of the recruiting process was agreed on by the consortium with a joint timeline and a template for the uniform appearance of job advertisements has been circulated by the Coordinator. In this template the eligibility criteria (Art. 6, GA) were emphasized and the recruitment and working conditions obligations (Art. 32, GA) were closely monitored by the Coordinator.

Adequate time (two months) has been allowed between the date of publishing an ESR post and the closing date for receipt of applications.


The following course of the recruiting process has been followed:

1. **Review of Applications:** The applications were sent to the Project Coordinator who forwarded them to the recruiting Institutions (primary supervisor) where a first screening of applications took place. Applications to more than one position were possible (and suggested in the advertisements) and should contain an indication for the order of preference (1st, 2nd or 3rd choice).
2. **Check of Eligibility:** after the application deadline, all applications have been screened according to the Marie-Curie eligibility criteria by the project Coordinator and by the recruiting institutions. In particular, suitable candidates have to be eligible according to the *ESR status* and the *Mobility Rule* (as detailed in the *Guide for Applicants*).
3. **Selection Phase at each Institution:** Following the standard procedures at each recruiting institution, three or four potential candidates were shortlisted and invited to job interview. According to individual agreements between the involved partners three/four potential candidate have been interviewed by a Committee at the host Institution or by video link if candidates were not able to travel. The Committee included the supervisors of the ESR, other members of the host Organization and the Project Coordinator or his representative.
4. **Final decision:** After a pre-selection of ESR-candidates a subcommittee of 5 supervisors from AUTH, IUSS, JSI, UPD, and URV selected the final candidate for each individual research project in consultation with the host Institution(s). The decision with an explanatory statement were sent to the Coordinator. Afterwards all candidates received a confirmation of the outcome of the recruitment process.

All project partners, though, followed a similar process for advertising and filling the ESR positions, following a strict equal opportunity policy.

2.3 Applications received and Gender Assessment

The consortium received applications from 55 applicants in total for the 14 ESR positions from which 25 were female (i.e. 45%). In total, beneficiaries shortlisted and invited ca. 40 candidates for interviews. We have received applications from 21 different countries, the distribution of the home

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countries of the candidates can be found in Figure 1. The majority of applications came from Greece (8), India (7), Italy (6), Pakistan and Spain (5) and Slovenia (3).

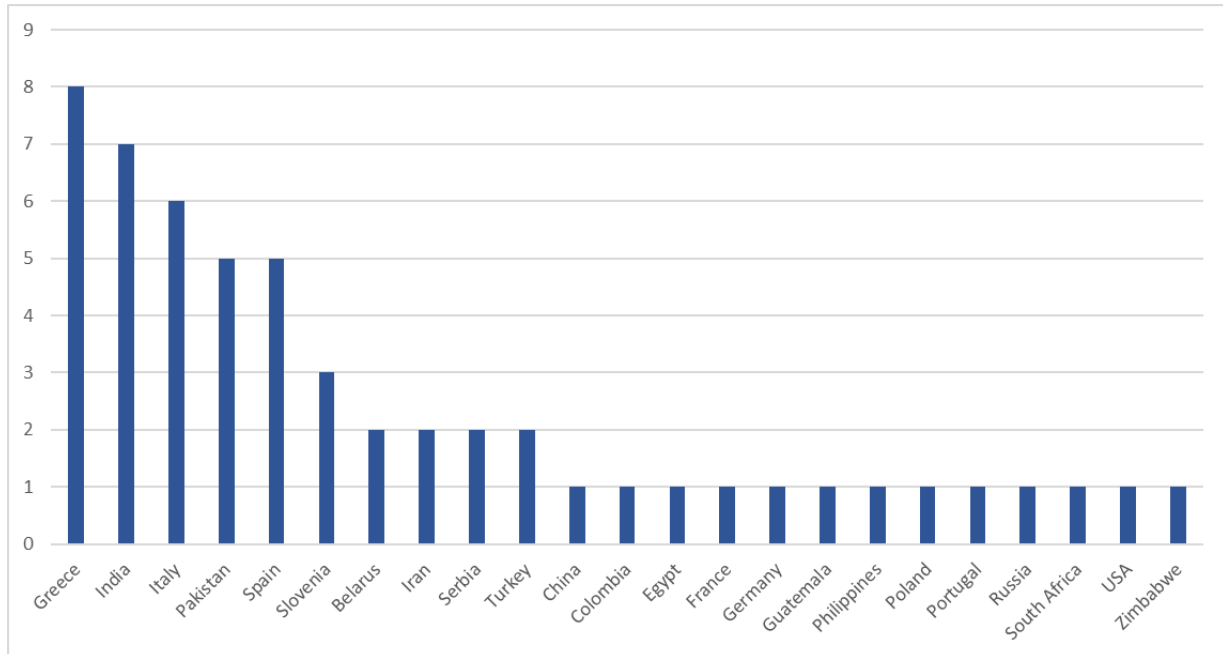



Figure 1: Distribution of home countries of applicants

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3 Recruitment Results

3.1 Selected Candidates

Fourteen very promising candidates were finally selected for the ESR positions in the NEUROSOME project. For an overview of the selected candidates and their start in the project, see Table 1. Eight of the fourteen ESRs were recruited by December 2018. Five of the selected ESRs come from non-EU countries (1 from India, 1 from Turkey, 1 from Russia, 1 from Iran and 1 from Guatemala) and needed visa before they could start their work in the project.

3.1.1 Gender

From the fourteen selected ESRs, seven are female and seven are male, this means that currently 50% of the ESRs are female. Each partner applied gender and equal opportunity policies at their local organizations for evaluating, selecting and interviewing the candidates. To ensure the equality of opportunities we have strongly encouraged women with the appropriate qualifications to apply.


3.1.2 Eligibility

The eligibility of the recruited candidates was verified by the recruiting organization and the project coordinator at AUTH. All the recruited candidates, at the time of the recruitment, were in the first four years (full-time equivalent research experience) of their research careers and have not been awarded a doctoral degree, hence qualifying as Early-Stage Researchers. Also, they all undertake transnational mobility, and have carried out their main activities outside the country of the recruiting organization for more than 24 months in the three years immediately prior to their recruitment. The eligibility criteria were verified by the detailed CVs and certificates provided by the selected candidates (enrollment certificates, certificates of Master degree or equivalent, etc.).

3.1.3 Nationality

The fourteen selected ESRs have the following nationalities:

- Greece (ESR1, ESR2, ESR10, ESR13, ESR14)
- India (ESR9)
- Italy (ESR5)
- Spain (ESR8)
- Slovenia (ESR7)
- Iran (ESR12)
- Turkey (ESR4)
- Germany (ESR6)
- Guatemala (ESR3)
- Russia (ESR11)

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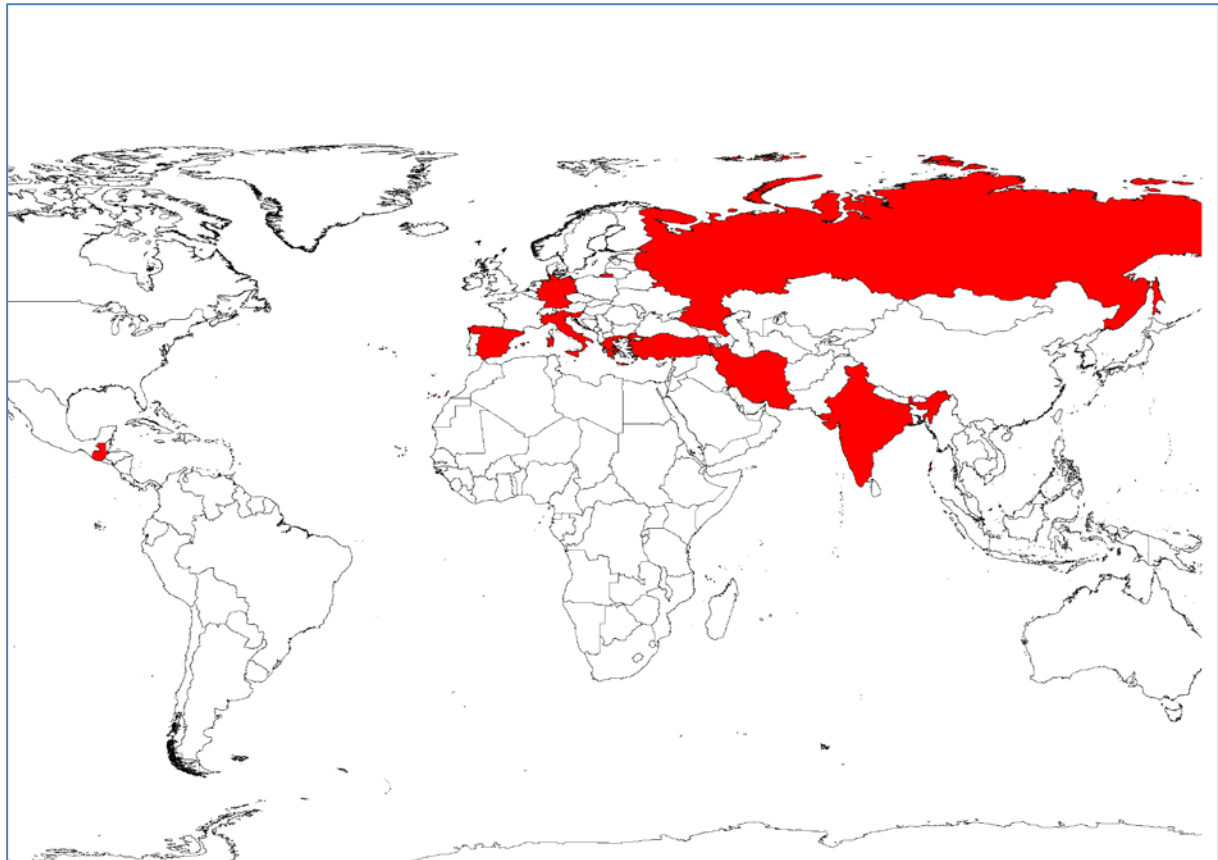



Figure 2: Distribution of home countries of recruited ESRs

Table 1: Selected ESRs for the fourteen positions in the NEUROSOME project

ESR	Last Name	Gender	Nationality	Recruiting Beneficiary	Recruitment Start Date
ESR1	Antonios Stratidakis	M	Greece	IUSS (IT)	1 January 2019
ESR2	Kokaraki Venetia	F	Greece	IUSS (IT)	1 January 2019
ESR3	Byron Francisco Fuentes Juarez	M	Guatemala	ISS (IT)	4 February 2019
ESR4	Öykü Dinçkol	F	Turkey	ISS (IT)	15 March 2019
ESR5	Marco Capodiferro	M	Italy	CSIC (ES)	1 October 2018
ESR6	Agneta Runkel	F	Germany	JSI (SI)	8 October 2018
ESR7	Tine Bizjak	M	Slovenia	JSI (SI)	8 October 2018
ESR8	Lorena Lopez Suarez	F	Spain	UPD (FR)	1 January 2019

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ESR9	Deepika	F	India	URV (ES)	22 February 2019
ESR10	Ioannis Petridis	M	Greece	AUTH (GR)	19 September 2018
ESR11	Vazha Dzhezheia	M	Russia	AUTH (GR)	28 November 2018
ESR12	Ramin Rezaee	F	Iran	AUTH (GR)	28 November 2018
ESR13	Ourania Anesti	F	Greece	TP (GR)	1 October 2018
ESR14	Irene Fragkiadoulaki	F	Greece	BURLO (IT)	21 December 2018

3.1.4 Candidates profiles

ESR1

Name: Antonios Stratidakis


Institution: University School of Advanced Studies-IUSS

Supervisor: Professor Dimosthenis Sarigiannis



I graduated in the Department of Materials Science, University of Patras, Greece in 2014. During my Bachelor studies I participated as an exchange student at Uppsala University, under the Erasmus European Program. In 2016 I obtained my Master's Degree entitled "Advanced Polymeric and Nanostructured Materials", University of Patras. During my MSc studies I gained a Scholarship funding under the European Program "Development in Industrial Research and Technology", while I also worked as a teaching assistant. During 2016-early 2019 I was a member of the Laboratory of Toxicology, Department of Medicine, University of Crete, Greece, working under a Research Project entitled "Development of novel polymeric carriers for controlled release of Indomethacin. *In-vivo* and *In-vitro* control in ophthalmic models". My research activity mainly extends in environmental pollution, toxicology and neurotoxicology.

My research project in NEUROSOME focuses on developing an integrative biology approach for developing AOPs for neurodevelopmental disorders. With the use of several bioinformatics tools I will create systems toxicology hypotheses from human data, with emphasis on inter-organ system changes and with the use of bioinformatics algorithms I will identify the common nodes across several pathways perturbed from co-exposure to organic and metallic compounds. My goal is to identify the most critical regulatory pathway nodes that regulate the onset of pathways beyond cellular homeostasis-thus identify potential candidates for adverse outcome pathways.

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ESR2

Name: Kokaraki Venetia

Institution:Institute for Advanced Study

Supervisor: Prof. Dimosthenis Sarigiannis



I graduated in Department of Applied Mathematics at the University of Crete (Greece) in 2012. I also have a Master's Degree in Operational Mathematics in Department of Mathematics and Applied Mathematics at the University of Crete in 2014. I was a member of the research team of the project ASMOPH, 'Excellence I' entitled Analysis, Stochasticity and Climate Modeling Simulation Phase in Institute of Applied and Computational Mathematics (IACM). Within this project, my Postgraduate dissertation entitled "Stochastics and Monte Carlo simulations for the description of time series of drug concentration in the blood of volunteers" was conducted. I have good knowledge of programming languages such as C, Fortran and Matlab and statistical packages SPSS and R language. In addition, I worked in Laboratory of Toxicology and forensic Chemistry of University of Crete medical school for the past two years where I have conducted several projects of statistical analysis and risk assessment.

My research project in NEUROSOME focuses on developing the proper modelling framework for estimating population external and internal exposure to xenobiotics, aiming to link external exposure metrics used in association studies to internal dosimetry metrics used in different toxicological testing strategies and identified omics signatures. The work will include the development of lifetime generic physiology-based biokinetic (PBBK) models for humans and animal models, able to describe internal exposure on susceptible developmental stages. Also the model will take into account interaction of multiple chemicals (mixtures interaction) at the level of metabolism, including enzyme inhibition and mechanism-based inhibition.

ESR3


Name: Byron Francisco Fuentes Juarez

Institution:D. Environment and Health, Istituto Superiore di Sanità

Supervisor: Alessandro Alimonti and Flavia Ruggieri



My project in NEUROSOME, aims at the collation of exposure to heavy metals related HBM data since the very early developmental stages, providing an overview of the actual population exposure to different potentially neurotoxic metals. These data will be also used for the validation of the PBBK model developed in ESR2 project.

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ESR4

Name: Öykü Dinçkol

Institution: Centre for Behavioral Sciences and Mental Health, Istituto Superiore di Sanità

Supervisor: Dr. Gemma Calamandrei



My research project in NEUROSOME focuses on identifying the in vitro and in vivo effects of co-exposure to metals. My research aims at characterize the neurobehavioral phenotype of murine models of exposure to multiple environmental stressors in pregnancy.

ESR5

Name: Marco Capodiferro


Institution: Institute of Environmental Assessment and Water Research (IDAEA), Spanish Council for Scientific Research (CSIC)

Supervisor: Dr. Joan O. Grimalt



I obtained my Master's degree in "Neurobiology" and my Bachelor's degree in "Biological Science – Genetic & Molecular curriculum" at Sapienza University in Rome, Italy. Also, I have completed a 18- month traineeship in the "Center for Behavioral Science and Mental Health" at the Istituto Superiore di Sanità (ISS) in Rome. During my academic studies, I attended several international seminars, workshops and conferences about neurotoxicology and neuroscience in general. Moreover, I followed different courses inherent to neuroscience that expanded my knowledge and improved my technical and practical skills.

My research within the NEUROSOME project is focusing on the analysis and evaluation of neuro-pollutants present in environmental samples from different media. My aims is to assess contamination levels of environmental means with which the studied population comes into contact, such as air, soil, water, settled dust and several food items either through the food web (metals, pesticides, POPs) or through food contact materials (plasticizers). Furthermore, I will pay attention on the role of neuro- pollutants on human health and environment in different biological samples coming from specific contexts.

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ESR6

Name: Agneta Runkel

Institution: Jožef Stefan Institute

Supervisor: Prof. Dr. Milena Horvat



I completed my Bachelor studies at the University of Bonn, Germany in Biology and Geography including a six-months Erasmus exchange at the National University of Ireland Maynooth. For my master's degree I joined the international study program Global Change Ecology at the University of Bayreuth, Germany. During that period, I completed a six months Erasmus traineeship in analytical chemistry at Stockholm University, Sweden and a three months internship at the Jozef Stefan Institute, Ljubljana, Slovenia. While studying in Bayreuth, I worked at the department of microclimatology and completed a science school on disturbance driven island ecology on La Palma, Canary Islands, Spain.

The aim of the PhD within the NEUROSOME project is to collect human samples from Mediterranean populations, select appropriate matrices and develop the methodology to assess the exposure levels of selected organic contaminants. This includes working with existing databases as well as targeted and non-targeted analysis of organic compounds.

ESR7

Name: Tine Bizjak


Institution: Jožef Stefan Institute

Supervisor: dr. Branko Kontić



I obtained my Master's degree in General Toxicology and Environmental Health Risk Assessment at the University of Eastern Finland, Kuopio. I finished my Bachelor's degree in Environmental Sciences at the University of Nova orica, Slovenia. Moreover, I have completed two 6 month Erasmus+ traineeships in Norway and Finland. In parallel with my studies, I have been working part time as a consultant in the field of toxicology. I have also worked as a research assistant in the field of aerosol science, focusing on the simulated atmospheric aging of combustion missions (i.e. black carbon) for several months.

My research within the NEUROSOME project is focusing on the interaction of science to policy. My aims are to demonstrate the usefulness and benefits of integrating Health Impact Assessment (HIA) with environmental (SEA, EIA) and other assessments (SA, CBA, CEA) at strategic level of development planning and decision making for the purpose of improving the public health status. Additionally, I will focus on the evaluation and clarification of the Human Biomonitoring data value and importance in the context of exposure assessment.

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ESR8

Name: Lorena LopezSuarez

Institution: Université Paris Descartes

Supervisor:Prof. Xavier Coumoul



I obtained my bachelor degree in Biology at Universitat de Barcelona, Spain. During my degree, I did an internship in Oryzon Genomics, working in the genetic improvement of crops. I then obtained a Postgraduate Certificate in Education, and I worked as a science teacher until 2016, when I joined the international master program MSc Brain Sciences at University of Glasgow, Scotland. As part of this program, I did my research project in Dr Linington lab (Glasgow), studying the role of FGF2 in the neuroprotective factors expression in astrocytes in the context of neuroinflammation.

My research within the NEUROSOME project is focused on the development of central nervous system cellular valid models to study the effects of several environmental pollutants on neurodevelopment, and, by treating this cellular models with different environmental representative mixtures chemicals, identify the mechanism of action through which they exert their neurotoxicity.

ESR9

Name: Deepika


Institution: Universitat Rovira i Virgili

Supervisor: Dr. Marta Schuhmacher



I have a Master's degree in Pharmaceutics (2014-2016) from Indian Institute of Technology, Banaras Hindu University, Varanasi, India. I completed my bachelor's degree from Guru Gobind Singh Indraprastha University, New Delhi, India (2010-2014) and was given gold medal for standing first in the university. Also, I was awarded academic excellence award for my outstanding performance during bachelor degree. I worked as a Scientist (Formulation Development- Topical Drug Delivery) in Dr. Reddy's laboratories Ltd., India. I applied research experience of nearly 3 years in drug development (semisolid dosage forms like topical products, micro emulsion, liposomes, Nano particulate drug delivery) & personal care products (hair care). I was awarded with breakthrough contribution award (2017-2018) for innovation in Dr. Reddy's Labs.

My objective in NEUROSOME is to develop the multimedia environmental exposure model for estimating contamination level of media (air, water, soil, food web, settled dust), indoor exposure and food items and to validate it under different scenarios taking into account the parametric uncertainty. The strategy also includes development of an integrative modelling framework taking into account environmental exposure, internal exposure, biochemical interaction and biological response to assess the neurotoxic effect of chemicals mixture and to have a wider picture of the exposome and related health outcomes.

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ESR10

Name: Ioannis Petridis

Institution: Aristotle University of Thessaloniki

Supervisor: Prof. Dimosthenis A Sarigiannis



I received my Bachelor's degree in Computer and Electrical Engineering, at the University of Thessaly, Greece. I completed my Master's degree in Biomedical Engineering at the Technical University of Delft, Netherlands. After that, I joined "Athena" Research Institute for a 2-month internship and then the decentralized European agency CEDEFOP for a 9-month traineeship. At the same time, I wanted to further develop my analytical skills by remotely pursuing a second Master's degree at the Open University of Cyprus.

My project for NEUROSOME will focus in the development of Quantitative Structure Activity Relationships (QSARs) and Physiologically Based Biokinetic (PBBK) models with a special interest in compounds relevant to neurodevelopmental disorders. My research will also include analysis of omics data using regression and clustering methods in R, Python and Matlab. Analysis using Artificial Neural Networks will be also investigated.

ESR11

Name: Vazha Dzhezheia


Institution: Aristotle University of Thessaloniki

Supervisor: Prof. Dimosthenis A. Sarigiannis



I obtained my Bachelor's degree in Chemical Technology at Moscow Technological University (MIREA) and my Master's degree in Chemical Technology at Dmitry Mendeleev University of Chemical Technology of Russia. During my Master's degree I gained a broad knowledge of chemical laboratory operating procedures and data analysis techniques. I also attended several international conferences about advances in safety, toxicology and ecology.

My task in NEUROSOME is to combine information from relevant environmental contamination data, HBM data and personal sensors data to develop robust human exposure models. During this project, analysis of multiple types of environmental and human samples will be done using different analytical chemistry techniques (e.g. GC-MS/MS, ICP-MS, HPLC-MS). Information from environmental contamination data will be combined with personal sensors data aiming at calculation of personal exposure.

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ESR12

Name: RaminRezaee

Institution: Aristotle University of Thessaloniki

Supervisor: Prof. Dimosthenis A. Sarigiannis



I graduated with a “PharmD” in Iran and I have been working in the field of pharmacology and toxicology as a research assistant. I have published over 70 original/review articles most of them in well-known journals of the field. I am familiar with using animal handling and behavioral tests, cell culture and molecular assays (western blotting and PCR), chromatography techniques for determination of contaminants in different matrices and risk assessment. During the last years, I, as an ERT (*European Registered Toxicologist*) have been collaborating with several journals as a reviewer and was recently assigned as an associate editor for “*Toxicology Reports*”.

My mission in NEUROSOME is to identify the molecular signatures (transcriptomics and metabolomics) of co-exposure to neurotoxicants, in biosamples collected from the population studies to understand the response of co-exposure to multiple stressors at the different levels of biological organisation. Transcriptomics will examine neural differentiation-related gene expression following exposure to mixtures of most commonly found combinations of neurotoxicants, and metabolic studies will be done in urine and blood samples.

ESR13

Name: Ourania Anesti


Institution: ToxPlus SA.

Supervisor: Prof. Aristides Tsatsakis



I am a Doctor of Dental Science (DDS), specialised in endodontics with a MSc in oral biology from the National Kapodistrian University of Athens. I have a BSc and an MSc in homeopathic medicine from the International Academy of Classical Homeopathy and I am a certified Tomatis practitioner – level 2. I have been practicing dentistry, endodontics and homeopathic medicine in my private practice for several years, an experience that gave me the opportunity to see from up close and from the clinician’s perspective how environmental, occupational and dietary factors impinge upon human health and onset or exacerbation of disease. For this reason, since 2016 I have been active in environmental health research collaborating with the University School of Advanced Study IUSS in Pavia, Italy and the HERACLES research center on the exposome and health at the Center for Interdisciplinary Research and Innovation of Aristotle University of Thessaloniki. I am currently a PhD student researcher at the Center for Toxicology and Forensic Science of the Medical School of the University of Crete under the supervision of Prof. A. Tsatsakis.

In NEUROSOME, I will work on something that will hopefully be the integrator of the results of other ESRs and other parts of the project. Namely, I will try to relate -omics, exposure and health

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outcome data using a combination of medical savvy and more formal ‘big data analytics’ approaches. My research will aim at unravelling the causal links between environmental exposure and disease developing and using a prototype methodology for carrying out genome-exposome-wide health association studies (GEHAS).

ESR14


Name: Irene Fragkiadoulaki

Institution:IRCCS Burlo Garofolo, Trieste - Italy

Supervisor: Luca Ronfani



In NEUROSOME, I will work on Genotyping, genome-wide analysis of cord blood samples collected from newborns participating in cohort studies. This will allow us to establish robust associations between health outcomes and gene polymorphisms implicated in neurodevelopment and /or response to xenobiotics.

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ANNEX 1 - CALL FOR APPLICATIONS



14 Early Stage Researcher positions in the field of "Neurological Exposome" in the EU- funded Marie Skłodowska-Curie Innovative Training Network (ITN) *NEUROSOME*

COORDINATING ORGANISATION

Aristotle University of Thessaloniki on behalf of the NEUROSOME consortium

RESEARCH FIELD

Computational biology, Genetic epidemiology, Bioinformatics, Systems biology, Metabolomics, Human biomonitoring, Behavioural toxicology, in vitro/in vivo testing, health impact assessment, environmental, exposure, GWAS, EWAS, personal sensors.

RESEARCHER PROFILE

Early Stage Researcher (ESR)

LOCATION

Multiple locations, see work locations below.

TYPE OF CONTRACT

Temporary

JOB STATUS

Full-time

INDICATIVE WORKING HOURS PER WEEK

40


EU RESEARCH FRAMEWORK PROGRAMME

H2020 / Marie Skłodowska-Curie Actions

MARIE CURIE GRANT AGREEMENT NUMBER

766251

We announce the start of the application period for **14 ESR** positions offered by the ten host organisations participating in the Innovative Training Network (ITN) "Exploring the Neurological Exposome (*NEUROSOME*)". The Marie Skłodowska-Curie Action "Exploring the Neurological

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Exposome (*NEUROSOME*) is an international research project, coordinated by Prof. Dimosthenis Sarigiannis from the Aristotle University of Thessaloniki (EL) and is financed under the funding line “excellent science” of the Horizon 2020 research and innovation programme of the European Commission.

NEUROSOME focus is on the investigation of causal associations among genetic predisposition, cumulative exposure to multiple environmental chemicals of children and neurodevelopmental disorders. The project brings together beyond- the-state-of-the-art advances in human biomonitoring and systems biology, exposure monitoring and toxicological testing technologies and advanced tools for computational analyses of the exposure-to-health effect continuum according to the exposome paradigm. The NEUROSOME methodology will be applied in population studies across different exposure settings to neurotoxicants (metals and selected organic compounds) in Europe. This will help us understand how environmental stressors lead to or exacerbate neurodevelopmental disorders. New standards for human biomonitoring data interpretation in conjunction with environmental and exposure information will be developed for ready use in chemical mixture risk assessment.


NEUROSOME seeks to train the next generation of exposome scientists able to tackle the global challenges associated with the impact on human health due to environmental exposure. Great emphasis is placed on training ESRs through collaborative exchanges and practical courses. The ultimate goal is to produce a new generation of exposome researchers, trained in academia, applied research and industry, with transdisciplinary skills (environmental end exposure modelling, human biomonitoring, in vivo and in vitro testing, -omics technologies, high dimensional bioinformatics and environmental epidemiology,) and understanding of fundamental science and its direct application to environmental health challenges.

Members of this **interdisciplinary and intersectoral scientific research network** acting as ESR **hosts** are:

- Aristotle University of Thessaloniki (EL), Coordination
- Istituto Superiore di Sanità (IT)
- Spanish Council for Scientific Research (ES)
- Jožef Stefan Institute (SI)
- University of Paris Descartes (FR)
- Universitat Rovira I Virgili (ES)
- ToxPlus SA (EL)
- Institute for Advanced Study (IT)
- Istituto di ricovero e cura a carattere scientifico Burlo Garofolo (IT)

The following institutions **take part in the network** and will **receive ESRs seconded from their host institution** for limited periods of time (between 6 and 10 months):

- Johns Hopkins University School of Public Health, Department of Environmental Health Engineering, Baltimore, MD, USA
- Emory University Rollins School of Public Health, Atlanta, GA, USA
- United States Environmental Protection Agency, Office of Research and Development

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/Human Exposure Modeling Branch, Research Triangle Park, NC, USA

- Harvard University, Department of Biomedical Informatics, Boston, MA, USA
- UPCOM SA, Brussels, Belgium

14 ESRs positions will be filled with a focus on the topics of neurodevelopmental disorders. All individual projects will have a duration of 36 months. Early stage researchers (ESRs) will be hired under a full-time, temporary contract at one of the host institutions. Their research would preferably lead to the awarding of a PhD in scientific domains relevant to environment and health science. The partners engaged in the project will work closely together, with each of the partners supervising at least one research project. ESRs will be trained through a structured and comprehensive programme and will not only learn the theory but will gain first-hand lab experience. All ESRs will spend time not only at the hosting institution but also in one of the other partner universities/research centers/regulatory agencies/companies involved in NEUROSOME throughout Europe and the USA.

Please find details about the application process and modalities at <http://www.neurosoma.eu>

We are looking forward to your application.

Best regards


Prof. Dr. Dimosthenis Sarigiannis

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Eligibility criteria

- You have a relevant university degree (master's degree or equivalent) in biomedical/bioinformatics sciences or biological sciences, life sciences or environmental/engineering science or related fields.
- You have excellent proficiency of the English language.
- Only applications that are complete, in English and in the right order, have been named as needed (SURNAME.pdf; avoid special characters) and that have been submitted by the deadline (**April 16, 2018**) will be considered eligible.
- The positions are open to all nationalities. However, your application has to comply with the European **Commission's Mobility Rules**, meaning that at the time of recruitment you must not have resided or carried out your main activity (work, studies, etc.) in the country of the host organisation for more than 12 months in the 3 years immediately before the reference date (indicative start of the employment contract, 1 May or June 2018). Compulsory national service and/or short stays such as holidays are not taken into account (European Commission's Guide for Applicants, p. 16).
- You are an **Early-Stage Researcher (ESR)**, i.e. in case you have already gained prior work experience in academia, you shall be in the first four years (full-time equivalent research experience) of your research career at the time of recruitment by the host organisation and have not been awarded a doctoral degree. Full-time equivalent research experience is measured from the date when you obtained the degree entitling you to embark on a

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doctorate, even if a doctorate was never started or envisaged. Part-time research experience will be counted pro-rata (European Commission's Guide for Applicants, p. 16).

- You cannot apply for more than three of the ESR positions, the research projects of which are listed in detail below.

Selection process

The selection committee will check applications against the following criteria:

- Scientific background and potential as indicated by candidate experience.
- Fit to a research project.
- Evidence of ability to undertake research.
- Evidence of working within groups or teams.
- Impact and benefit of the proposed training to the candidate's research career.

Gender equality and minority rights will be promoted in the selection process.

Three candidates will be short-listed for each research project and invited to an interview (interviews by video link will be held if candidates are not able to travel).

Interviews will consist of two parts: 1) a short presentation by the candidate followed by questions and answers, and 2) competence-based interview.

NEUROSOME is looking for a broad international representation of early stage researchers. The network clearly acknowledges its responsibility for the recruitment of the researchers, their working and living conditions, as stated in the document "The European Charter for Researchers - Code of Conduct for the Recruitment of Researchers".


ESR Projects description

Selected projects: Subproject Title (you can apply for a maximum of three projects):

- **ESR 1 - Functional integration of different omics results using bioinformatics tools towards development of AOPs for neurodevelopmental disorders (Host: Institute for Advanced Study , Pavia (IT)).**

Main objectives: To develop an integrative biology approach for developing AOPs for neurodevelopmental disorders building systems biology hypotheses based on multiple - omics data.

Expected Results: The project aims at training an ESR on integrative biology tools such as Agilent GeneSpring, Thompson-Reuters MetaCore™ and Reactome/Functional Interaction network plug-in for Cytoscape, so as to create systems toxicology hypotheses from human data, with emphasis on inter-organ system changes. Bioinformatics algorithms will be used to identify common nodes across several pathways perturbed from co-exposure to the compounds of interest to NEUROSOME (organics and metals). This is expected to allow the identification of the most critical regulatory pathway nodes that regulate the onset of pathways beyond cellular homeostasis - thus identify potential candidates for adverse outcome pathways. The critical question is whether there is a limited number of Pathways of Toxicity (PoT). It is likely that the number of critical cellular infrastructures is limited; thus the points of vulnerability, to which the PoT would converge, should also be limited, however, this

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is one of the major scientific questions to be answered within this project. ESR2 will work in close collaboration with ESR12 and ESR13.

- **ESR 2 - Development of an integrated exposure model coupled to PBBK model for mixtures of neurotoxicants (Host: Institute for Advanced Study , Pavia (IT))**

Main objectives: To develop the proper modelling framework for estimating population external and internal exposure to xenobiotics, aiming to link external exposure metrics used in association studies to internal dosimetry metrics used in different toxicological testing strategies and identified omics signatures.

Expected Results: The work will include the development of lifetime (including gestation and breastfeeding) generic physiology-based biokinetic (PBBK) models for humans and animal models (e.g. rodents), able to describe internal exposure on susceptible developmental stages. The model will take into account interaction of multiple chemicals (mixtures interaction) at the level of metabolism, including enzyme inhibition (e.g. competitive, non-competitive and uncompetitive inhibition) and mechanism-based inhibition. To cover a large chemical space and so to assure a more “generic” character of the model, biological properties (e.g. partition coefficients and metabolic parameters such as the maximal velocity (V_{max}) and Michaelis affinity constant (K_m) or the intrinsic clearance (V_{max}/K_m)) will be derived from advanced QSAR/QSPR accessory models, using both quantum descriptors and artificial intelligence techniques such as artificial neural networks. Validation of the PBBK model will be done using the data from the ESR3, ESR6 and ESR11 projects. Receiving input from ESR9 project (external dose estimation), is going to produce the internal doses relevant for in vitro testing (ESR4, and ESR8 projects).

- **ESR 3 - Human biomonitoring of toxic metals associated to neurodevelopmental disorders (Host: Istituto Superiore di Sanità, Rome (IT)).**


Main objectives: To identify the levels of internal exposure to toxic metals through human biomonitoring.

Expected Results: Studies have shown associations between exposure to environmental concentrations of individual toxic metals such as lead, mercury, arsenic, cadmium, and manganese and developmental outcomes in children, including reduced IQ and decreased performance on developmental tests. The simultaneous exposure of an individual to mixtures of chemicals, which may interact in an additive, synergistic, or even antagonistic way, remains to be explained and defined, especially in a mechanistic perspective. ESR3 project, aims at the collation of exposure to toxic metals related HBM data since the very early developmental stages, providing an overview of the actual population exposure to different potentially neurotoxic metals. These data will be also used for the validation of the PBBK model developed in ESR2 project.

- **ESR 4 - Targeted in vitro and in vivo testing of neurodevelopmental disorders focusing on exposure to toxic metals (Host: Istituto Superiore di Sanità, Rome (IT)).**

Objectives: To assess in vivo and in vitro models the neurodevelopmental toxicity of co-exposure to metals to identify omics biomarkers associated with the behavioural phenotype in peripheral and brain tissues.

Expected Results: Targeted in vivo studies in laboratory rodents will be performed to derive a set of peripheral accessible markers of susceptibility, vulnerability and effects, able to predict the effects in the brain and the neuropsychological outcome. To this aim, wild-type mouse strains or carrying common and potentially functional polymorphisms (SNPs identified by other partners in this network) will be used to verify the impact of varying

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doses of contaminants (heavy metals, alone or in combination), administered at different critical stage of development (pregnancy, infancy, adolescence). A battery of behavioural tests including evaluation of sensorimotor, social, emotional and learning/memory functions (mirroring those applied to evaluate infants' and children's development) will be performed at different life stages to identify both short- and long-term effects and evaluate the risk of aging-related impairments. In parallel, omics biomarkers (oxidative stress markers, , protein and metabolite levels and epigenetic markers) will be measured in peripheral organ/tissues and in the brain to evidence parallel changes and possible differences anchored to the behavioural phenotype, eventually to validate the peripheral biomarkers as indexes of abnormal brain and behaviour development. In vitro (using the novel iPSC-derived 3D BMPS) and in silico models based on the findings in the animal models will be tested out in collaboration with ESR2, ESR8 and ESR13.

- **ESR 5 - Development of analytical framework of environmental samples from different media towards exposome assessment (Host: Spanish Council for Scientific Research, Barcelona (ES)).**


Objectives: This Project is devoted to provide the needed relevant environmental contamination data for the compounds of interest for the exposure models to deploy the individual exposome.

Expected Results: The candidate will learn to review and collate relevant environmental contamination data for the compounds of interest. He also will be trained in several analytical chemistry techniques and instrumentation (GC-MS/MS, ICP-MS, HPLC-MS). The most advanced technologies for the targeted and untargeted analysis of trace pollutants will be available in this research group such as gas chromatography coupled to Q-exactive orbitrap mass spectrometry, and the equivalent method with liquid chromatography. In addition to these instruments, the partner has about 30 gas chromatography and liquid chromatographs coupled to electron impact MS, chemical ionization MS, time of flight MS, MS/MS and magnetic sector MS. The research work for development and training will also encompass methods for planning and implementing sampling, sample handling and analysis for environmental health association studies and for deploying the individual and population exposome. As a result, the knowledge gaps of environmental contamination for the different media will be identified and filled in by additional measurements in "fusion" to modelled data produced in WP4.2, providing as such a comprehensive picture of the contamination levels and the different synthesis of the neurotoxins "cocktails" of the populations of the different regions. ESR5 will be in close collaboration to ESR9 project.

- **ESR 6 - Analysis of human biosamples for biomarkers quantification (Host: Jožef Stefan Institute, Ljubljana (SI)).**

Objectives: To collect the biosamples from the selected population and to identify the exposure levels to mixture of organic compounds

Expected Results: This project aims at the collection of the biosamples from the cross Mediterranean (Greece, Italy, France, Spain, Slovenia and Croatia) populations to be investigated. The ESR will gain experience on how to design an exposome based population study, how to identify representative population, what type of matrices to select, how to store and preserve the samples and what protocols to follow regarding further analysis. Identification of exposure levels to mixtures of organic compounds will be carried out through chemical analysis of commonly used matrices (e.g. urine, blood, hair) providing estimates for exposure levels of selected organic contaminants (flame retardants, phenols, phthalates, etc.). The ESR will get familiar with a broad range of analytical chemistry

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techniques (GC-MS/MS, ICP-MS, HPLC-MS) and protocols for human biosamples sampling, storage, preparation and analysis, as well as with the development of analytical techniques for emerging compounds. ESR6 project will be in close collaboration with ESR2, since the exposure biomonitoring data will also be used for the validation of the PBBK model.

- **ESR 7 - Integration of Health Impact Assessment (HIA), sustainability appraisal and environmental impact evaluations with development planning emphasizing the role of Human Biomonitoring in ex-ante HIA (Host: Jožef Stefan Institute, Ljubljana (SI)).**

Objectives: To demonstrate usefulness of the integration of HIA with environmental and other assessments at strategic level of development planning (sustainability). To clarify and understand role and importance of HBM in the context of exposure assessment and the two types of HIA: ex-post and ex-ante.

Expected Results: HIA+SA+SEA+EIA+CBA+CEA and their integration are not crucial for the sake of their good practice and from the scientific point of view but rather to make them as effective and beneficial as possible in the context of improving public health status, and optimization of the development proposals. That is the reason why assessments need to be integrated with planning. This philosophy will guide research and work of ESR8; expectations are that ESR will develop advanced competence in the field of HIA working on both theoretical (conceptual) and practical issues. By combining work in WP4 and WP5 – collaboration among ESRs1, 2, 3, and 13 – the key results of the work of ESR7 are expected to be:


- advanced understanding of the needs for, and role of, analytical results of the quality/contamination of environmental media (air, water, soil) in ex-post and ex-ante HIA.
- capability of developing conceptual exposure models linked to concrete development planning proposals, e.g. long-term electric energy planning, transport in urban conglomerations (ex-ante HIA).
- optimization of development proposals based on comparative evaluation of alternatives using CBA and CEA, and considering potential exposure assessment.

ESR7 will work in close collaboration with ESR13

- **ESR 8 - Targeted in vitro analysis associated to neurodevelopmental disorders, focusing on organic environmental compounds (Host: University of Paris Descartes, Paris (FR)).**

Objectives: To identify response of the relevant nervous system cells to combined effect to environmentally relevant mixtures.

Expected Results: Suggested mechanisms of neurotoxic action for some of these chemicals include oxidative stress, epigenetic effects, disruption of cell signalling and endocrine disruption. Yet to date, no single mechanism can account for the neurological toxicity of this group of chemicals, which differ widely in structure, chemical properties and reactivity. It is reported here, however, that there is indeed a unifying explanation for the induction of neurological diseases by this diverse group of chemicals. The studies referred to above show that accumulation of all of these chemicals in body serum was associated with increased incidence of neurological impairment, neurodevelopmental diseases. Several of these chemicals are lipophilic and all were shown to accumulate in body serum (and probably in the lipophilic parts of the brain) following exposure. We will use several cell lines and primary cells to characterize the toxic effects of contaminant combinations: on the neuronal cells derived from iPS cells, glial cells and endothelial cells representative of the blood brain barrier (BBB). Moreover we shall use the novel iPSC-derived human 3D brain

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microphysiological system (BMPS) developed at JHU that comprises mature neuron and glial cells and presents spontaneous electrical activity and axon myelination. We will assess the effects of contaminant combinations on the major toxic pathways in those cells (AhR, NRF2, ER, PR, LXR, oxidative stress, etc.). We will also test the hypothesis that lipophilic chemicals could facilitate the absorption of hydrophilic compounds across the body's lipophilic membranes, particularly in BBB cells. It is proposed here that the lipophilia of these exogenous chemicals disorganizes lipophilic membranes including the blood brain barrier, leading to neurological disorders, thus enabling the entry for toxic hydrophilic species that would otherwise not be absorbed. Thus, in vitro testing of co-exposure to multiple lipophilic organic compounds in relevance to the compounds investigated in NEUROSOME is expected to contribute to the elucidation of the mechanisms resulting in neurological impairments and to the characterization of cross-talks between signalling pathways that are not characterized using single xenobiotics. Dosing for confirmatory in vitro analysis will be directed from the internal dose in target tissues calculated in the research project of ESR2.

- **ESR 9 - Development of multimedia environmental contamination and human exposure model (Host: Universitat Rovira I Virgili, Tarragona (ES)).**


Objectives: To develop a comprehensive multi-media environmental contamination model for estimating contamination levels of contact media (air, water, soil, food web, settled dust), indoor exposure and food items and validate it under different scenarios taking into account uncertainty.

Expected Results: The project aims at the development of an exposure modelling framework that encompasses the – multimedia model for assessing environmental contamination levels for different media where people are exposed to. Existing modelling schemes (ChemCAN, CalTOX, BETR Global model, CHEMGL, MUM-Fate and Simplebox) will be reviewed and evaluated. It is known that the complexity of these models ranges from relatively coarse multiple linear box models (MCMs) which assume homogenous landscape properties in each medium and assume that all environmental compartments are mixed, over spatial multimedia models (SMs) that are collections of single medium models in which the output of one model serves as input for the others, and spatial multimedia compartmental models (SMCMs) which consider one or more environmental compartments as non-uniform regions. Exposure estimation should include multi-chemical and multi routes estimation and validation of long term exposure dose using reverse dosimetry model. The critical uncertainties and/or oversimplifications will be characterized and properly addressed, in the newly developed computational model. The later will be based on the existing model INTEGRA. Validation of the model will be carried out based on the data collated and originally derived from Task 4.1, so high level of synergies with ESR5 are expected. This model will be incorporated to a wider human exposure model that will fuse advances in personal sensors technology and agent based modelling.

- **ESR 10 - Development of Quantitative Structure Activity Relationships for use in biokinetic models (Host: Aristotle University of Thessaloniki, Thessaloniki (EL)).**

Objectives: To development Quantitative Structure Activity Relationships for use in biokinetic models, with a special focus on compounds relevant to neurodevelopmental disorders.

Expected Results: A current limitation to further introducing PBBK models in the risk assessment arena is the lack of generic character of these models. A critical limiting factor of describing ADME processes for a large chemical space is the proper parameterization for

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“data poor” compounds. In order to expand the applicability of PBBK models to cover as much as possible the chemical space, model parameterization for data poor chemicals is done using advanced quantitative structure-activity relationships (QSARs). In silico approaches, including QSARs, are widely used for the estimation of physicochemical and biochemical properties, biological effects as well as understanding the physicochemical features governing a biological response. QSARs are described as regression or classification models, which form a relationship between the biological effects and chemistry of each chemical and comprise the activity data to be modelled, the data with which to model and a method to formulate the model. The approaches for predicting metabolic rates are basically related to CYP-mediated metabolism and focus on the identification of substrate specificity. Additional parameters to be modelled in order to be able to reliably apply a lifetime PBBK model include renal clearance, tissue:blood partition coefficient, placental transfer and blood-brain barrier; the latter is very important for the case of neurodevelopmental diseases. Preliminary investigation has shown that Abraham’s solvation equation combined with Artificial Neural Networks (ANN) is one of the most efficient methods for effectively predicting the parameters essential for a PBBK model. Predicted parameters for selected data poor chemicals will also be validated experimentally. ESR10 project is in very close link to ESR2 project, aiming at the development of a generic lifetime PBBK model for cumulative internal exposure.

- **ESR 11 - Advancing exposure assessment through environmental monitoring, human biomonitoring and use of personal sensors (Host: Aristotle University of Thessaloniki, Thessaloniki (EL)).**


Objectives: To develop exposure models based on the assimilation of environmental, HBM and personal sensors data.

Expected Results: The candidate will learn how to combine information from relevant environmental contamination data, HBM data and personal sensors data aiming at developing robust human exposure models. ESR11 project will rely on the analysis of multiple types of environmental samples (air, soil, water, settled dust, food items) as well as human specimens (urine, hair), thus training in several analytical chemistry techniques and instrumentation (GC-MS/MS, ICP-MS, HPLC-MS) will be required. Information from environmental contamination data will be combined with personal sensors data aiming at calculation of personal exposure. The latter will be validated against HBM data. Associations among these types of data will be investigated, aiming to identify the way environmental data and HBM data should be sampled, in order better reflect human exposure. It is expected that different recommendations will be derived, based on the physicochemical properties of the different compounds, depending on their persistency in the environment and human body as well. ESR11 will be in close collaboration with ESR2, ESR3, ESR6 and ESR9.

- **ESR 12 - Transcriptomics, metabolomics and toxicity pathway analysis of combined exposure to neurotoxicants (Host: Aristotle University of Thessaloniki, Thessaloniki (EL)).**

Objectives: To identify the molecular signatures (transcriptomics, metabolomics) of co-exposure to neurotoxicants, aiming at pathway analysis

Expected Results: The biosamples collected from the population studies will be further analysed, in order to understand the response of co-exposure to multiple stressors at the different levels of biological organisation. Transcriptomics will be evaluated in order to identify responses aiming at neural differentiation-related gene expression to mixtures of most commonly found combinations of neurotoxicants, which are expected to vary among

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the different regions (Greece, Italy, Spain, Slovenia and Croatia) included in the study. Differences in the metabolic signatures from urine and blood samples among the subjects of the populations to be investigated will be explored, aiming to further differentiate the profiles of healthy and non-healthy individuals. These two types of data will set the basis of toxicity pathway analysis for the health outcomes of interest. This will be analysed using advanced bioinformatics tools such as GeneSpring by Agilent and the outcomes of this project will be in close collaboration to ESR1 and ESR13 projects.

- **ESR 13 - Development of “big data” analytics approaches and their use to relate -omics, exposure and health outcome data (Host: ToxPlus SA, Heraklion (EL)).**

Objectives: To develop advanced methods for big data analytics, such as methods for multi-output classification/regression. To collate and organize existing omics, exposure and health outcome data (related to neurodevelopmental disorders). To apply the developed methods to the data and find genome-exposome-wide health associations.


Expected Results: Unravelling the causal links between environmental exposure and disease is the ultimate goal of exposome-related studies. The development and use of the methodology for carrying out genome-exposome-wide health association studies (GEHAS) will be carried out within the ESR13 project. Multiple indicators (e.g., clinical scores) of health/disease status will be considered (both separately and jointly).

The ESR13 will develop methods for predictive modeling and feature ranking (marker discovery) in the context of multiple outputs (health outcomes). These will be based on existing approaches to multi-target regression and classification. It will also collate and coherently store multiple types of data (environmental, exposure, biomonitoring, multi-omics, toxicological testing), e.g., via NoSQL (Not only SQL). For assessing environmental exposure contribution to neurodevelopmental disorders, internal doses will be coupled to health impacts on the local population through the methods developed by this ESR. The internal doses will be derived from the measured biomarker, quantified in different biological matrices, estimated by the application of the lifetime generic PBBK model. This will correspond to the biological effective dose in the target tissue, which is consistent with the measured biomarker level. To estimate the health impacts, multi-output regression will be used, accounting for the different covariates (age, sex, socio-economic status etc.). This ESR project will link internal doses (calculated in ESR2 project) with health effects or intermediate biological events (as identified in ESR1 project) that can be associated to health perturbations through pathway analysis (ESR1 and ESR12 projects) considering the interdependence of the covariates (using as metric an analogy of the “linkage disequilibrium” metric used in genome-wide association studies).

- **ESR 14 - Genome-wide profiling and identification of single nucleotide polymorphisms (SNPs) relevant to susceptibility to neurodevelopmental disorders (Host: Istituto di ricovero e cura a carattere scientifico Burlo Garofolo, Trieste (IT)).**

Objectives: To identify the different polymorphisms that affect the response to exposure to chemical agents towards metabolic and neurodevelopmental disorder.

Expected Results: Common gene variants may induce susceptibility to environmental factors by increasing or decreasing physiological responses to adverse effects from environmental toxins, through the mother’s internal or external environment. Much research has been devoted to find SNPs that may help predict an individual’s susceptibility to environmental pollutants, and risk of developing particular diseases. With regard to neurodevelopmental disorders, it has been found that same alleles from two single-

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nucleotide polymorphisms (rs3785143 and rs11568324) genetically predispose for attention-deficit hyperactivity disorder (ADHD). Beyond the SNPs that increase population susceptibility to neurodevelopmental disorders, there are SNPs affecting the metabolism of xenobiotics, increasing in this way the biologically effective dose and the overall effects of environmental exposure. For examples SNPs in genes involved in the detoxification of environmental pollutants have been found in some individuals with Autism Spectrum Disorders (ASD). Members of families CYP1, CYP2, and CYP3 —especially CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 in liver—metabolize about 95% of xenobiotics. In order to better understand the way exposure to xenobiotics results in disease, we need to investigate the involvement of genetic susceptibility parameters in real low-exposure scenarios. This project will focus on genome-wide analysis of cord blood samples obtained from newborns originally enrolled in the PHIME cohort (about 1200 subjects). This will allow us to establish robust associations between health outcomes and gene polymorphisms implicated in neurodevelopment and /or response to xenobiotics. The outcomes of ESR14 project will provide significant input in the development of the generic biokinetic model (ESR2 project), as well as ESR1, ESR12 and ESR13 projects.