Qu'est-ce que le dispositif ExposUM Doctoral Nexus ?

Les Doctoral Nexus proposés par l'Institut ExposUM sont des réseaux de 3 à 4 doctorantes et doctorants, issus de disciplines différentes et affiliés à au minimum deux unités de recherche différentes.

Par rapport à une thèse classique, participer à un Doctoral Nexus favorisera la capacité à travailler en équipe et à concevoir des projets de manière transdisciplinaire tout en approfondissant son propre champ d'expertise.

Un programme pédagogique spécifique sera proposé et les doctorant(e)s concerné(e)s auront également l'opportunité d'organiser un séminaire au sein du réseau Nexus.

Les thèses sont financées d'emblée pour 4 années, comprenant le salaire du doctorant ou de la doctorante ainsi qu'une enveloppe d'environnement.

Sujet de thèse **Impact of external exposome focusing on air pollutants on cardiorespiratory health under real-life conditions**

Directeur de thèse : KASE TANNO Luciana
C-supervisor: Isabella Annesi Maesano
UMR: UMR 1318: Desbrest Institute of Epidemiology and Public Health, University of Montpellier -INSERM, France

Part of Project NEXUS 2024 EXPAIR (Development of innovative sensors for measuring EXPosure to pollutants in AIR to unravel cardiorespiratory effects)- Transdisciplinary collaboration between Electronics Institute (IES) and two medical research laboratories.

Rational:

Worldwide, respiratory conditions such as chronic obstructive pulmonary disease (COPD), asthma, pulmonary fibrosis, lung cancer, etc. contribute to a substantial burden on healthcare systems and patients' and families' quality of life, which has to be attributed to environmental hazards. In the EU, 1 in 8 deaths are caused by lung diseases, and numbers are rising. Ever since the Global Burden of Disease report revealed that air pollution is responsible for a significant proportion of respiratory morbidity and mortality, air quality has become a public health priority for governments, clinicians, patients and the general population [Annesi-Maesano, 2021]. As a consequence, on the one side a better comprehension of respiratory effects of air pollution has become an urgent need

and on the other side respiratory patients are increasingly asking pulmonologists about the effects of air pollution on their respiratory disease and about how air pollution can be avoided. Epidemiological or fundamental research on the impact of air pollution on respiratory diseases to satisfy these needs is difficult for two major reasons. First, the composition of the atmospheric air is highly complex, with many hazardous air pollutants interacting together, which cannot easily be taken into account. Second, individuals spend a large majority of their time indoors (up to 90% in Western countries), and air quality monitoring networks and air pollution dispersion models cannot provide information on indoor exposure at the personal level. For these reasons, high resolution assessments, including at the individual level, are required. Low-cost air quality sensors (LCSs) are receiving increasing attention as they promise a revolutionary advancement in air quality monitoring by offering the potential for more precise spatial and temporal scales, enabling individual-level assessment of air quality real-life exposure to relate it to health conditions [Laguille, 2020]. To date, there is little published work in relation to respiratory health using wearable air pollution LCSs [Sesé, 2023].
PhD thesis 3 will use sophisticated sensors from PhD thesis 1 (IES) in stationary position as well as the mobile Canarin remote sensor [Dessimond, 2022], in mobile position to assess individual exposure to various air pollutants in real life taking the spatio-temporal dimensions into account and relate these exposures to respiratory parameters through an exposomic approach [Cecchi, 2018].

Aims:

- To evaluate how subjects drawn from the general population are exposed to a variety of air pollutants (benzene, formaldehyde, PM, CO, VOCs) and comfort parameters (T, Hum, CO_2) in real-life using fixed and mobile sensors (at the individual level the latter) and how their exposure evolves in time.
- To evaluate at the individual level in real time exposure taking the spatio-temporal dimension (every 15 minutes at GPs location) into account to PM, CO, VOCs and comfort parameters through a portable sensor (Canarin).
- To evaluate the relationship of exposure to air pollutants and comfort parameters to respiratory clinical parameters through an exposomic approach

Methods:

Subjects: Volunteer participation of 50 professionals and 50 students of the Faculty of Medicine of the University of Montpellier. They will be their own controls over the study (cross-over study design). They will attend 3 medical visits (one every 8 months) to monitor evolution of air pollution exposures and respiratory health.
Survey:
Step 1: The sensors generated by Thesis 1 will be placed at places of the buildings of the Faculty of Medicine of the University of Montpellier considered as representative of exposure in order to evaluate levels of Benzene, CO, 2 weeks before the visit.
Step 2: Each participant will be invited to carry a remote sensor, the previously mentioned Canarin, for 2
weeks before each of the 3 planned visits. The "Canarin" is a validated medical device

allowing to follow in a geolocalized way (GPS) and over time (every 15 seconds) the exposure to fine particles of less than 10 micrometers "PM10", less than 2.5 micrometers "PM2.5" and those of less than 1 micrometer "PM1", to Volatile Organic Compounds "VOCs" (total and isolated to be decided according to PhD thesis 1's choice, as well as to follow the ambient temperature and the humidity rate of the ambient air.
Step 3: During the 3 visits, the subjects will fill a sociodemographic /clinical/epidemiological (risk factors and behavior) questionnaire and undergo clinical evaluation with: tension measure, oxymetry, cardiac frequency, spirometry, weight, height, FeNO.

Cardiovascular outcomes:
Resting heart rate and blood pressure will be assessed at each visit. In addition, heart rate variability (ratio LF/HF) will be assessed during 5-minute resting ECG monitoring using a connected Polar device.
Respiratory outcomes:
Lung function testing, FeNO, oxymetry, cardiac frequency at each visit as in routine pneumological visits. The inhaled dose will be also assessed considering air pollutant concentrations, exposure duration, breathing rates (through an App), and individual susceptibility.
Exposome implementation:
At IDESP where the PhD 3 will be conducted, we have worked to define the elements that should be collected for a complete assessment of the specific and general external exposome to be related to respiratory health using standardized questionnaires, tools and models. The questionnaires chosen have been used and validated in other cohorts (notably E3N, an epidemiological study of almost 100,000 MGEN women followed over 30 years, ECRHS, a longitudinal epidemiological cohort of around 20000 individuals, some having developed respiratory diseases, EDEN, a longitudinal epidemiological cohort of around 2,000 pregnant women successively followed-up, HEALS and EAT2). Tools and models are being used in other IDESP's epidemiological survey. More precisely the following hazards to be related to individual health status will be assessed:

a) specific assessments: ¨ diet, food supplements (Constance questionnaires), eating behavior (DEBQ, TFEQ-RC16, SCOFF, IES-2, Constance, EDEN, ECRHS)¨ smoking and toxic substances (Constance questionnaires, ECRHS), ¨ physical activity (ECRHS, IPAQ and Nutrinet questionnaires), ¨ allergens and household biocontaminants (ECRHS, EDEN, ISAAC questionnaires, IDESP Source- Exposure Matrix for Indoor Environments), ¨ occupational exposure (job-exposure matrix),¨ social profile, stress, psychological trauma and quality of life (Hamilton scale, CTQ, CAPS scale, STAI questionnaires, Cohen's preconceived stress, QIPS, PCL, PCS, WCC and quality of life).

b) general assessments by geocoding of addresses of the participants: ¨Airborne pollutants (particulate matters [PM10 and PM2.5], nitrogen dioxide (NO_2), and ozone (O_3)) using the CHIMERE model (promoted by INERIS). ¨ Airborne endocrine disruptors (as for example dioxins, cadmium, PCB and BaP), based on a detailed inventory and geolocation of emission sources in France, in Occitanie in particular, and the CHIMERE model, estimating up the hourly concentrations of major air pollutants PCB and BaP in whole France. ¨ Foodborne endocrine disruptors (as for example dioxins, cadmium,

PCB and BaP), assessed by the linkage between a dietary questionnaire and the second French total diet study (EAT2).

Overall, major environmental hazards, composing the external exposome, will be assessed and considered in the establishment of the proper role of the considered air pollutants.

Statistical and epidemiological analysis:

Descriptive analysis and series analysis of air pollution exposures and respiratory health outcomes data during the 3 visits, separating indoor and outdoor exposure. In this context, health indicators representative of the cardiorespiratory evolution across the visits will be developed and validated with PHYMEDEXP. EnvWAS (Environment-wide Association Study) methods will be used to evaluate the association between external exposure to pollutants though the fixed and mobile sensors (QEPAS and Canarin respectively) and clinical respiratory outcomes. To better consider the air pollution effect, the inhaled dose will be estimated based on heart rate and ad hoc equations and considered.

PhD thesis students 3 will be in charge of the recruitment of participants, distribution of devices, visits with clinical evaluation and collection and analysis of data generated over the 3 steps of the project. Steps 1 and 2 can start in parallel.

PhD3 will be in regular communication with PhDs 1 and 2. Outcomes of the Thesis 2 performed in animal model can be extrapolated to human evaluation proposed in PhD Thesis 3.

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Duration: 4 years

Formation expected:
Diploma in Medicine, Master 2 or equivalent grade in epidemiology, statistics.

Skills:

- Applied knowledge of Medicine: perform clinical history, assessment of heart rate and blood pressure, perform lung function testing, measure FeNO, oxymetry, cardiac frequency
- Computering: instrumentation, modelisation (ray tracing, finite elements…), exposomic evaluation
- Autonomy, scientific rigor, organization, project management, ability to synthetise, writing and presentation skills.
- Having previous publications will constitute an added value.
- English level: B2-C1 minimum

Modalités de candidature

La candidature doit être composée des éléments suivants :

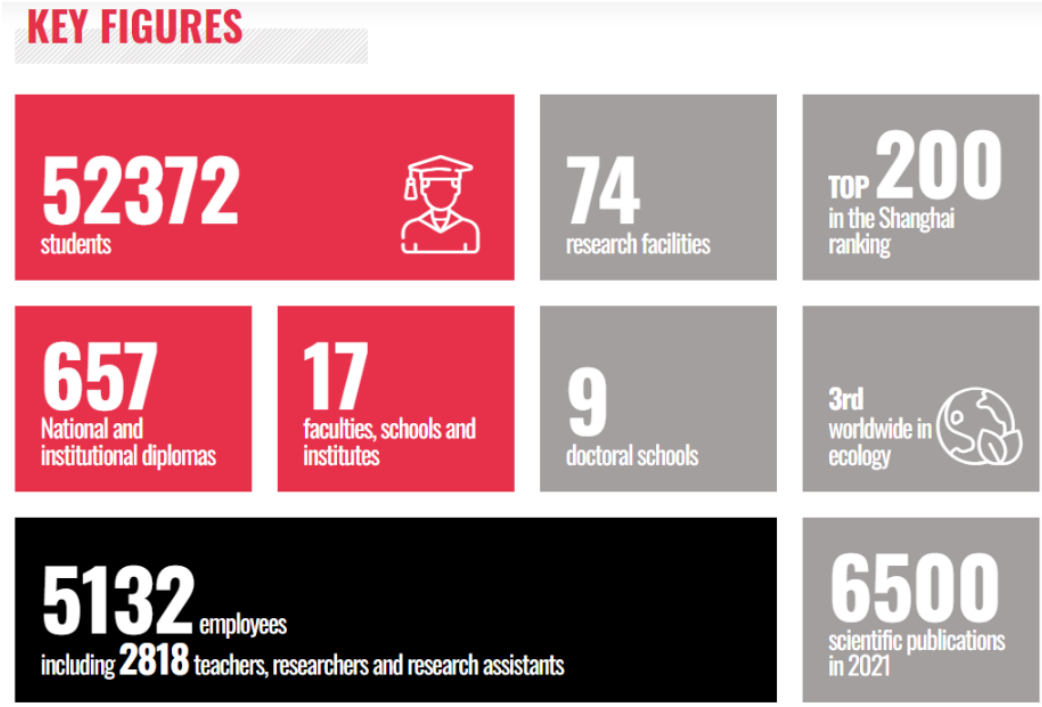
- Un CV
- Une lettre de motivation
- De la copie du diplôme permettant l'inscription

- Des éléments spécifiques demandés par l'école doctorale CBS2 (https://edcbs2.umontpellier.fr/index.html?language=fr&page=home)

Si vous souhaitez postuler sur ce sujet, adressez au plus vite un mail à luciana.tanno@gmail.com et isabella.annesi-maesano@inserm.fr en mettant en copie aurore.vicet@umontpellier.fr et exposum-aap@umontpellier.fr afin de les informer de votre intérêt.

Avant le dimanche 21 avril, 20h CET

The University of Montpellier



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