ISRCTN24225493 https://doi.org/10.1186/ISRCTN24225493

EXIMIOUS: Investigating the impact of exposures (exposome) on the immune system (immunome)

Submission date 10/12/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 01/02/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 04/03/2024	**Condition category** Other	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Depending on our lifestyle, diet, work and social environments, we all experience a different and complex set of exposures throughout our lifetime. The combination of these is defined as the exposome. EXIMIOUS is a European research project and cohort study that aims to develop a new way of assessing the human exposome, to better understand the factors that lead to exposure-related immune effects at different stages of people's lives.
By unravelling the connections between our immune system (the immunome), our genetic material (the genome) and the environment, EXIMIOUS will help put in place the right preventive actions and policies to safeguard the individual, group and population well-being.

Who can participate?
Participants are recruited in (a) occupational settings, (b) hospital settings and (c) general and birth cohorts. The EXIMIOUS cohorts are predefined.

What does the study involve?
Several measurements will be taken from participants, from biological measurements (blood, urine) to environmental samples (air pollution, dust, …). Participants will also be requested to complete a common EXIMIOUS questionnaire and – in some cases – an occupational exposure interview.

What are the possible benefits and risks of participating?
The EXIMIOUS project aims to improve people's lives by gaining insight in exposure-induced immune effects. We believe that the potential for disease prevention is huge. (Auto)-immune disorders are very invalidating and require lifelong medical care. By gaining knowledge on the impact of the exposome on the immunome, we will be able to identify at risk individuals, groups and populations. Based on this knowledge we can then advise preventative measures that target these individuals or groups.
No risks are associated with participation.

Where is the study run from?
Katholieke Universiteit Leuven (Belgium)

When is the study starting and how long is it expected to run for?
January 2020 to June 2025

Who is funding the study?
European Commission

Who is the main contact?
Prof Peter Hoet, peter.hoet@kuleuven.be
Dr Manosij Ghosh, manosij.ghosh@kuleuven.be
Katrijn Broothaerts, katrijn.broothaerts@kuleuven.be

Contact information

Type(s)
Scientific

Contact name
Prof Peter Hoet

ORCID ID
https://orcid.org/0000-0002-0292-6603

Contact details
Environment and Health
ON I bis Herestraat 49 - box 706
Leuven
Belgium
3000
+32 16 330197
peter.hoet@kuleuven.be

Type(s)
Scientific

Contact name
Dr Manosij Ghosh

ORCID ID
https://orcid.org/0000-0001-5034-001X

Contact details
Environment and Health
ON I bis Herestraat 49 - box 706
Leuven
Belgium
3000
+32 16 37 76 98
manosij.ghosh@kuleuven.be

Type(s)
Public

Contact name
Ms Katrijn Broothaerts

Contact details
Environment and Health
ON I bis Herestraat 49 - box 706
Leuven
Belgium
3000
+32 16 33 00 45
katrijn.broothaerts@kuleuven.be

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
874707

Study information

Scientific Title
Mapping exposure-induced immune effects: connecting the exposome and the immunome

Acronym
EXIMIOUS

Study objectives
Changes in the immune system are the result of a person’s lifetime exposure and we can use this information to predict the development of disease. At the level of the individual, we will identify ‘immune fingerprints’ that integrate the lifetime exposure. The overall objective of EXIMIOUS is to bring about a new way of assessing the human exposome by combining innovative ways of characterizing and quantifying multiple environmental exposures (exposomics) and mapping exposure-induced immune effects (immunomics). New bioinformatics tools will be developed through the use of systems biology, artificial intelligence, and machine learning that will first combine and then analyze the datasets that link exposome, immunome, and other omics data with clinical and socio-economic data of individuals. By exploring the entire pathway from exposome, to immune fingerprint, to disease during a person’s lifetime (including prenatal exposures) we will better understand the factors that lead to exposure-related immune effects at different stages of people’s lives. In addition, we will pinpoint the most critical types of exposure and the individuals/groups bearing the highest risk in order to put in place the right preventative actions and policies at the individual, group and population levels.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 30/08/2021, The Medical Ethics Committee of the UMFST (University of Medicine, Pharmacy, Science and Technology 'GE Palade' of Targu-Mures, Gheorghe Marinescu 38, Tirgu Mures, Mures, 540142, Romania; +40 265 215.551; no email provided), ref: nr. 1455 din 30.08.2021
2. Approved 20/08/2021, Clinical Research Ethics Committee from the Vall d'Hebron Hospital (Passeig de la Vall d'Hebron, 119, 08035 Barcelona, Spain; +34 934 89 30 00; no email provided), ref: PR(AG)595/2020
3. Approved 18/11/2021, Comité d'éthique Hospitalo Facultaire de l'UCLouvain et des Cliniques Universitaires Saint Luc (Promenade de l'Alma 51 bte B1.43.03, 1200 Bruxelles, Belgium; no telephone number provided; commission.ethique-saintluc@uclouvain.be), ref: 2021/21SEP/388
4. Approved 03/07/2019, KU Leuven (Herestraat 49, 3000 Leuven, Belgium; +3216332211; no email provided), ref: S61777
5. Approved 15/10/2007, The Medical Ethical Committee (Medisch Ethische Toetsingsingscommissie, University Medical Center Groningen (UMCG), The Netherlands; +31 50 – 361 4204; no email provided), ref: M07.052740; 09/080U-B3712010785; 15/035U-B371201524537; CME2021/030

Study design
Observational case-control study

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Immune fingerprints as signs of environmental exposure

Interventions
The observational study will include quantification of exposure (chemical, biological and physical agents), measurement of high-dimensional immune cell signatures and soluble proteins, genetic-epigenetic, and miRNA changes, and data will be integrated and interpreted using Statistical and systems immunology approaches.

In the EXIMIOUS project, we aim to identify immune fingerprints as signs of environmental exposure (biomarker). Ideally, these early signs can be picked up before health is harmed, to help prevent diseases in individuals in the general population and/or in workers with a specific type of exposure. We will extensively collect clinical and socio-economic data as well as information on the environmental exposure (exposome) and the health status of the immune system (immunome), of participants from several cohorts—covering the entire lifespan, including prenatal life. We will follow two approaches, one starting from the exposome and the other starting from the disease. These approaches will 'meet in the middle'.

Several measurements will be taken from participants, from biological measurements (blood, urine) to environmental samples (air pollution, dust, …). Participants will also be requested to

complete a common EXIMIOUS questionnaire and – in some cases – an occupational exposure interview.

Intervention Type
Other

Primary outcome(s)
Objective 1: delineating the exposome
Type of data:
- Environmental sampling
1.1 Air pollution measures (including Volatile organic compounds (VOC))
1.2 Air pollution data from monitor stations
1.3 Dust measures (mineral and metal dust, textile dust)
1.4 Chemicals in occupational environment (solvents, Pesticides)
1.5 Organics (microplastics, polymers, mycobacteria, fungi)
- Questionnaires
1.6 Questionnaires about living habits (smoking, food intake, ...) and other demographic information (sex, age, employment, education, geographic,…)
1.7 Questionnaires about current and past exposures (at work and at home)
- (Personal) Biomonitoring Sampling
1.8 Biological samples (blood cells and plasma, urine (black carbon, metals, VOC), ...)
Source of data:
- Environmental sampling of current exposures in different cohorts (feasible in all cohorts except for DOC*X and LifeLines cohort; the focus will be on occupational cohorts)
- Modelling of environmental exposure (all cohorts)
- Biomonitoring on biological samples from different cohorts (patients and controls, waste workers (Denmark + Romania), LifeLines Cohort, ENVIRONAGE cohort)
- Clinical interviews about current and past exposures (All disease cohorts and their controls)
- Questionnaires about current and past exposures (feasible in all cohorts except for DOC*X and LifeLines cohort)
- Information about traffic indicators and residential greenness, temperature, humidity, UV, sunlight (ENVIRONAGE cohort)
- Hyperspectral images acquired from environmental sampling and its data processing. This consists of raw ENVI files for hyperspectral images, classification images (.png) and statistical data about the spectral data and the machine learning models generated.

Objective 2A: immunomics
Type of data:
2.1 Biological samples: whole blood, mononuclear blood cells, blood plasma, urine samples, bronchoalveolar lavage (BAL), lymph node cells, DNA extracted from blood cells, buccal cells, nails, saliva
2.2 Clinical data: clinical information about the patient, HRCT thorax (imaging), pulmonary function results (PFT), serology results, bronchoalveolar lavage (BAL) results, histopathology results (when available), specific inhalation challenge results (when available), ECG results, other testing on other organs (when available)
2.3 Other: DEXA, retinal photographs, carotid ultrasounds, heartrate, body size measurements
2.4 Questionnaires
2.4.1 Questionnaires about living habits (smoking, food intake, ...) and other demographic information (sex, age, employment, education, geographic, …)
2.4.2 Questionnaires about current and past exposures (at work and at home)
Source of data:

- From all cohorts: existing biological samples are used where possible, new biological samples are collected, analysed or biobanked
- From newly diagnosed patients (and controls), and workers: biological sampling (e.g. sarcoidosis patients, waste workers, park workers)
- Clinical information from electronic patient notes in hospital (UZ Leuven for patients with sarcoidosis, Hospital Vall d'Hebron for patients with hypersensitivity pneumonitis due to exposure to avian and fungal proteins)
- Other data from existing cohorts (ENVIRONAGE, Sarcoidosis patients versus controls, patientswith hypersensitivity pneumonitis due to exposure to avian and fungal proteins)
- Questionnaires about current and past exposures (feasible in all cohorts except for DOC*X and LifeLines cohort) -

Objective 2B: multi-omics:
Type of data:
2.5 Epigenetics analysis: DNA methylation and microRNA analyses (genome-wide methylation data, miRNA expression profiling data)
2.6 Genomic analysis using GWAS analysis approach
2.7 Telomere length measurement (Leucocyte telomere length)
2.8 Exosome analysis (characterization of cellular secretome)
Source of data:
- Biological samples from multiple cohorts: existing biological samples are used where possible, new biological samples are collected

Key secondary outcome(s))
There are no secondary outcome measures

Completion date
30/06/2025

Eligibility

Key inclusion criteria
General Adult population
1. At least 18 years old
2. Written informed consent must be obtained before any assessment is performed

Birth cohort
1. Participants are recruited at the birth of their child. Enrollment of eligible women is performed during all four seasons.

Occupational study population
1. Occupational exposure to one of the exposures: mineral dust and/or organic solvents at selected workplaces (UMFST – Romania); Waste workers with a high diversity of microorganisms (NRCWE – Denmark); Park workers in the city of Barcelona (VHIR – Spain)

Control group of office workers, matched to age and gender.
1. At least 18 years old
2. Written informed consent must be obtained before any assessment is performed

Disease cohorts
1. Clinically active cases of sarcoidosis or Systemic sclerosis (KU Leuven), Systemic sclerosis,

Systemic Lupus Erythematosus and Rheumatoid arthritis (UCL), active hypersensitivity pneumonitis (VHIR) or AID (Note: patients are recruited in the following hospitals: University hospital of Leuven, University hospital of Louvain, Vall d'Hebron University Hospital)

Control group for disease cohorts
1. At least 18 years old
2. With or without treatment
3. Written informed consent must be obtained before any assessment is performed

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria
General Adult population:
1. Immunomodulator / immunosuppressive treatments

Birth cohort:
1. Not being able to fill out a questionnaire
2. Not a singleton pregnancy
3. Having a planned caesarean section

Occupational study population
1. Younger than 18
2. Pregnancy
3. Unwillingness or inability to wear air samplers, and fill-out questionnaire-based health surveys
4. Immunomodulator / immunosuppressive treatments
5. Less than 1 year of employment to the selected workplaces

Disease cohorts
1. Younger than 18
2. Specific criteria may include wearers of metal prostheses (sarcoidosis), or Previous diagnosis in case of hypersensitivity pneumonitis

Date of first enrolment
01/01/2022

Date of final enrolment
31/12/2024

Locations

Countries of recruitment

Belgium

Denmark

Romania

Spain

Study participating centre
KATHOLIEKE UNIVERSITEIT LEUVEN
Oude Markt 13
Leuven
Belgium
3000

Study participating centre
UNIVERSITEIT HASSELT
Martelarenlaan 42
Hasselt
Belgium
3500

Study participating centre
UNIVERSITE CATHOLIQUE DE LOUVAIN
Place de L'Université 1
Louvain La Neuve
Belgium
1348

Study participating centre
DET NATIONALE FORSKNINGSCENTER FORARBEJDSMILJO
Lerso Parkalle 105
Kobenhavn
Denmark
2100

Study participating centre
FUNDACIO HOSPITAL UNIVERSITARI VALL D'HEBRON - INSTITUT DE RECERCA
PASSEIG VALL D HEBRON 119-129 EDIFICIO

Barcelona
Spain
08035

Study participating centre
UNIVERSITATEA DE MEDICINA, FARMACIE, STIINTE SI TEHNOLOGIE DIN TARGU MURES
GHEORGHE MARINESCU 38
Targu Mures
Romania
540139

Sponsor information

Organisation
European Commission

ROR
https://ror.org/00k4n6c32

Funder(s)

Funder type
Government

Funder Name
European Commission, Directorate-General for Research and Innovation (DG RTD)

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		01/02/2022	21/11/2022	Yes	No
Other publications	SOP for collection, storage and shipment of biological samples		07/02/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	All project related results and publications are available here		04/03/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes