Pinpointing Novel Targets of Air Pollution in Human Olfactory System and Brain

A Data Management Plan created using DMPTuuli

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Project abstract:

Air pollution is a life-long health concern affecting individuals of all ages. Whilst effects of air pollutants on the cardiovascular and respiratory systems are well-characterised, how neurodegeneration results from long-term exposure to polluted air remains unclear. It is speculated that chronic neuroinflammation drives loss of cellular function in the brain. However, the immune-privileged organ will not exhibit signs of inflammation until irreversible damage occurs. In addition, this field of research is hindered by sparse availability of cells and tissue for clinically-relevant studies. Therefore, the need for novel targets of air pollution may be addressed by investigating metabolic mechanisms in cells, which is also implicated in several sporadic neurodegenerative diseases including Alzheimer's disease. This multidisciplinary project proposes to study how air pollutants affect cell metabolism in two key clinically-relevant systems, the olfactory system and the brain. This will be achieved first, by comprehensive metabolic profiling of specific cell types and then, developing functional models that recapitulate the systems in vivo. The scientific impact lies in revealing unprecedented 3D models and novel mechanistic consequences of air pollution. An impact beyond academia is to raise environmental awareness of air pollutants and neurodegenerative diseases, a growing global health burden. Both published findings and our preliminary results revealed mitochondrial dysfunction in patient-derived olfactory cells and mouse neural cells after exposure to air pollutants. Specifically, enzymatic activity in olfactory cells showed reduced capacity to meet maximum energy demand, depleted ATP pool and resilience to the cytotoxic effect of the pollutants. In conclusion, pinpointing novel targets in mitochondrial function will present new knowledge on how environmental factors lead to non-hereditary neurodegeneration as well as improve early detection and therapeutic intervention. The findings in this project are important for providing science-based evidence to potential regulation of ultrafine air pollutants to improve the environment and human health.

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1. General description of data

1 September 2019 - 31 August 2022

work package 1	work package 2	work package 3
In vitro experimental data (excel)		Animal cognitive tests (excel)
Clinical data (excel)	In vitro experimental data (excel)	Behavioural test results (excel)
Sequencing data (FASTQ)	Live microscopy data (tiff)	Live 3D microscopy data (tiff)
Microscopy data (tiff)		

Data sets are quantitative. Majority of the data generated are experimental and clinical data will be used in one of the three work packages proposed in the project. Raw quantitative data are recorded in Excel whilst images are generally stored as TIFFs, unless otherwise stated in the research methods. In addition, clinical data from anonymised patients detailing olfactory capacity and disease progression will be analysed. For statistical analysis, experimental data will collected in 3 to 6 technicial replicates of a minimum of 4 biological replicates, each experiment will be carried out in triplicates, where possible.

From the clinic (Clinical data are anonymised)

- Olfactory and cognitive test results from healthy patients and patients with Alzheimer's disease.
- Diagnostic results from nasal biopsies and blood including disease progression and gender
- Records of cell lines established from nasal biopsies (in excel format)

Reuses: anonymised clinical data may be published in open-access journals in conjuction with experimental data.

Experimental

- Quantitative data from in vitro assays of cell lines (in excel format)
- Microscopy images (in tiff format, unless otherwise stated)
- sequencing data (in fastq format)
- Qualitative data from behavioural tests in mouse (in excel format)
- Statistical analysis (Graphpad or SPSS)

Reuses: sequencing data will be deposited in public repositories. in addition, all experimental data will be published in open access journals where data can be requested by other research groups.

Ensuring consistency

- Standard operating protocol for collecting data will be established by the principal investigator, for data that is collected by individuals besides the principal investigator.
- Data will be collected by only the principal investigator and a PhD student involved in the project
- Data will be analysed by the principal investigator
- Clinical data will be collected by the same collaborators.

Ensuring quality

- Imaging data will be collected at the highest resolution.
- Sampling sizes will be verified by UEF statistians to allow for analysis
- Where necessary, raw data will be shared with collaborators for optimal analysis and transparency in result presentation.
- Statistical outliers will be highlighted, where necessary.

2. Ethical and legal compliance

Clinical data will be anonymised prior to analysis. Therefore, the project will handle data from anonymised patients. The patients have given their consent to the use of clinical data collected and they are free to withdraw their consent at any point during the project and relevant data will be deleted. Consent from the group leader will be granted prior to sharing or publication. Some of the clinical data and all experimental data will be deposited in public repositories and published in open-access journals. Data will be shared with collaborators only upon consent.

Patient data are coded, i.e. made anonymous to confirm the protection of personal data. Only information on the disease stage, age and test results of the patients open to the applicant and the research tem members. All new study subjects recruited during this project will provide informed consent to donate biopsied olfactory mucosa and blood samples. Shortly, the subjects or their trustees are informed orally and in written of the aims, procedures, objectives and potential hazards of the study and of how their clinical data and biological samples are going to be handled. The subjects can refuse donating tissues and are allowed, at any point of the study, to withdraw their consent without any consequences. This project will yield no benefit for the individual donating the samples. All materials will be collected and handled according to the national ethical guidelines and guidelines for Good Clinical Practice.

Ownership of data, copyright and IPR are duly managed by the A.I. Virtanen Institute, University of Eastern Finland. Clinical data such as disease stage and in vitro data from patient cell lines can be shared by collaborators listed in the license (insert license number). It is unexpected that there are copyrights and other restrictions preventing the sharing of data.

3. Documentation and metadata

All data will be documented in both a password-protected electronic lab notebook as well as in a hard-copy lab notebook with archival ink. Metadata are recorded as per the following.

1) Project, experiment, name of person carrying out the experiment,date of experiment, technical and biological repeat numbers

2) Type of raw data, sample sizes, file size, collection method, analytical method

3) Raw data (various) and statistical analysis (Graphpad), exact locations in stand-alone work station and UEF cloud storage

4) Location in public repositories, if any.

4. Storage and backup during the research project

The data from all in vitro experiments are stored in the investigator's UEF-registered work station and backed up in the UEF cloud storage (up to 1Tb) which are password-protected. In addition, all non-sensitive raw data are also backed up in DVD-ROMs, external hard drives and in written form in laboratory notebooks for long-term storage for the life cycle of the project and projects in relevant consortia. All clinical data are stored in a standalone work station with limited access and password protection. In addition, anonymised clinical data will be stored in the UEF cloud only accessible to the investigator and her group members. If necessary, selected external collaborators will be granted access to such data.

The principal investigator and the group leader will be solely responsible for controlling access to all data for the project. Access to specific data is limited to collaborators listed in the funding application and protected by password.

5. Opening, publishing and archiving the data after the research project

Quantitative data, NGS data, anonymised clinical data and images

Analyses of these data sets will be openly available when they are included in publications. Raw data will made available upon request. NGS data will be deposited in renowned public repositories following publication in open-access journals. Anonymised clinical data as well as the metadata will be deposited in relevant repositories, if any.

Data that are expected to have long-term value include clinical data of patients with Alzheimer's disease and mild cognitive impairment. This will comprise of in vitro experimental data, sequencing data, behavioural test results. As all data are electronic copies, they will be archived in external hard-drives and in the UEF cloud with password-protection (up to 1Tb for non-sensitive data, and up to 50Gb for sensitive data). Experimental data will be stored for at least 3 years following the end of the project life, whilst data recorded in lab notebooks will be archived for as long as the research group exists in the present institute. Clinical data will be stored for as long as required by projects carried out in the research group and with patient's consent.

Experimental data be collected throughout the duration of the project every few days per week throughout working

months. Ad-hoc analysis is performed as and when collection of the data set is completed. Concurrently, the meta-data is generated and all complete data sets are archived in the investigator's UEF-registered stand-alone work station and backed up to the UEF cloud and in a password-protected external hard-drive for long-term storage. As annual publication is planned between 2019 and 2022, relevant data sets will be finalised for manuscripts at least the month before submission. Desposit of data in public repositories will only be done after publication in open-access journals.