UNCOVERING ADVERSE HEALTH EFFECTS OF ATMOSPHERIC POLLUTANTS

EMPIR EURAMET
The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

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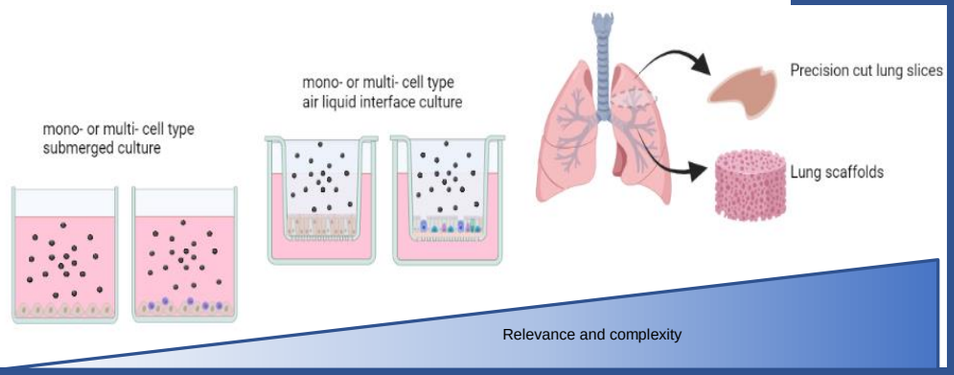
Background

- Exposure to atmospheric pollution has been linked to a range of **acute and chronic health conditions** and results in an estimated **seven million deaths annually**.
- Exposure limits for inhalable particulate matter (PM) are based primarily on **particle size**, however there is poor correlation between size-based exposure limits and subsequent **adverse health outcomes**, hindering the development of **effective**, targeted **air quality guidelines.**
- The **complex mixture** of components (gases and aerosol particles) in **real world air**, makes it challenging to assess the health impacts of constituents based on epidemiological data.
- By contrast, ***in vitro* studies** based on controlled exposure of biological respiratory model systems to **well-characterised references aerosols** offers the potential to develop a deeper, mechanistic understanding how cells and tissues are affected by airborne pollutants.

Aims

Quantify the cytotoxic effects of aerosols by:

1. Applying more **realistic biological models,** such as re-cellularised human lung scaffolds, which better mimic the *in vivo* environment.
2. Exposing respiratory models to well-defined laboratory-generated **reference aerosols** using methods that imitate real world aerosol inhalation.
3. Performing **multimodal imaging and biological assays** to analyse exposed samples, obtaining different measurements of specific responses.
4. Exploring correlations between the properties of the particles and their downstream **toxicological effects**.



Methods

We have applied a combination of high-resolution imaging techniques and biomedical assays.

Light sheet fluorescence microscopy has allowed us to visualise the architecture of thick sections of re-cellularised healthy and exposed lung scaffold models.

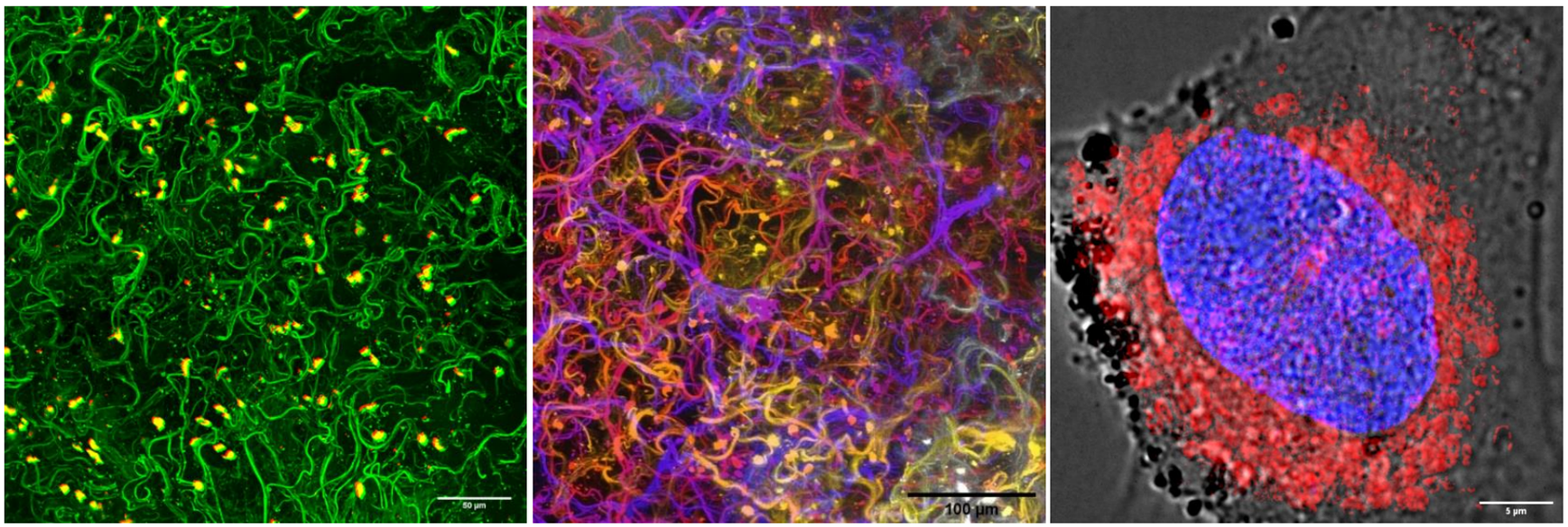
Super-resolution techniques enabled us to capture structural changes in subcellular organelles (i.e. mitochondria) in response to PM exposure.

Transmission electron microscopy was used to capture images of the different particulates for analysis of size and distribution, as well as exposed cells images for correlation with super-resolution images.

Biomedical assays such as plate reading-based fluorescent assays allowed us to obtain metabolic activity, cytotoxicity and reactive oxygen species responses.

Analysis and correlation of these datasets using various computational methods and comparison against bulk toxicity data will allow us to better understand how specific PM constituents give rise to an adverse biological response linked to acute and chronic health conditions.

Results



Light sheet fluorescence microscopy images of lung tissue scaffold (Left) Human fibroblast cells (red/yellow) are visible within the scaffold (green). (Middle) Colour depth projection showing the 3D architecture of the tissue. (Right) Super resolution image of an alveolar basal epithelial (A549) cell in submerged exposure to carbon PM (black spots), mitochondrial structures stained red and cell nucleus stained blue.

Conclusions & Impact

- Multimodal imaging techniques permitted **visualisation of cells** and **subcellular structures** in a variety of *in vitro* respiratory model systems which will help us to probe the effects of exposure to airborne pollutants.
- Quantitative image analysis combined with results of biomedical assays will provide detailed transformational insights into the **mechanisms underlying respiratory toxicity** and ultimately lead to more pertinent air quality guidelines.

References

WHO, Ambient air pollution: A global assessment of exposure and burden of disease, 2016

Acknowledgements

This work was funded by the EMPIR programme (project AeroTox, 18HLT02), which is co-financed by the Participating States and the European Union's Horizon 2020 research and innovation programme