UK Health Security Agency

SAQN STFC AIR QUALITY NETWORK

NIHR | Health Protection Research Unit in Environmental Exposures and Health at Imperial College London

UKRI Science and Technology Facilities Council

Understanding how inhaled particles impact the brain-blood-barrier (BBB)

Chang Guo[1], Andy Ward[2], Sanghamitra Mukhopadhyay[3], Laura Zanetti Domingues[2], Robert Lees[2], Esther Garcia Gonzalez[2], Benji Bateman[2], Rachel Smith[1], Tim Gant[1], Ian Mudway[4]

[1] *Radiation, Chemical and Environmental Hazards Directorate, UK Health Security Agency (UKHSA), Oxfordshire, OX11 0RQ, UK*

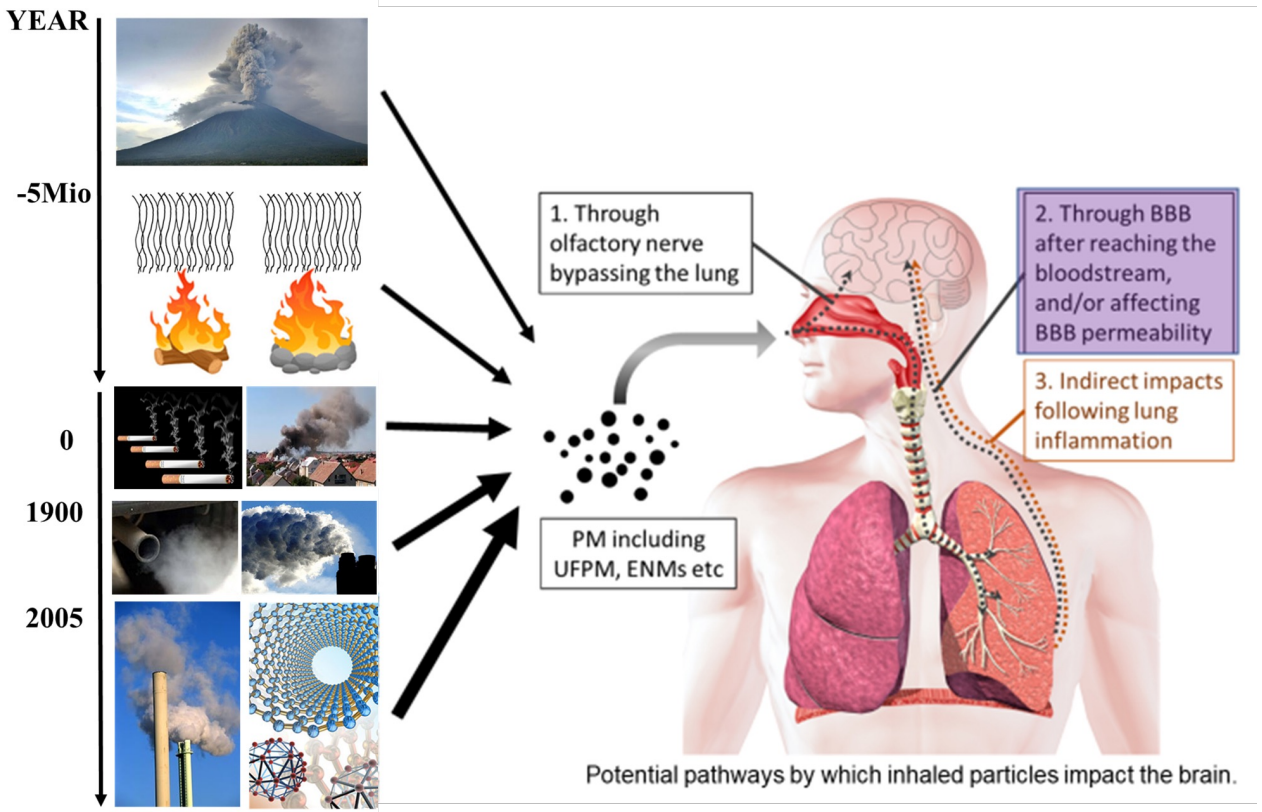
[2] *Central Laser Facility (CLF), Science and Technology Facility Council (STFC),*

[3] *ISIS Neutron and Muon Source, STFC,*

[4] *Environmental Research Group, School of Public Health, Faculty of Medicine, Imperial College London; and MRC Centre for Environment and Health, School of Public Health, Faculty of Medicine, Imperial College London;*

Clean Air Networks Conference 5-6 July

Background



Potential pathways by which inhaled particles impact the brain.

- 50 million people live with dementia and this number is expected to triple over the next 30 years.
- The economic impact of dementia is significant. In the UK, the total cost of dementia is £34.7bn and will rise further to £94.1bn by 2040.
- In the 2020 update report of the Lancet Commission on Dementia Prevention, Intervention, and Care, air pollution was one of the three newly added modifiable life-course risk factors for dementia.
- COMEAP has identified the need to perform more mechanistic research to understand the potential and route by which particles reach the brain.

Cell biology assays

- **Cytotoxicity by modified LDH assay**

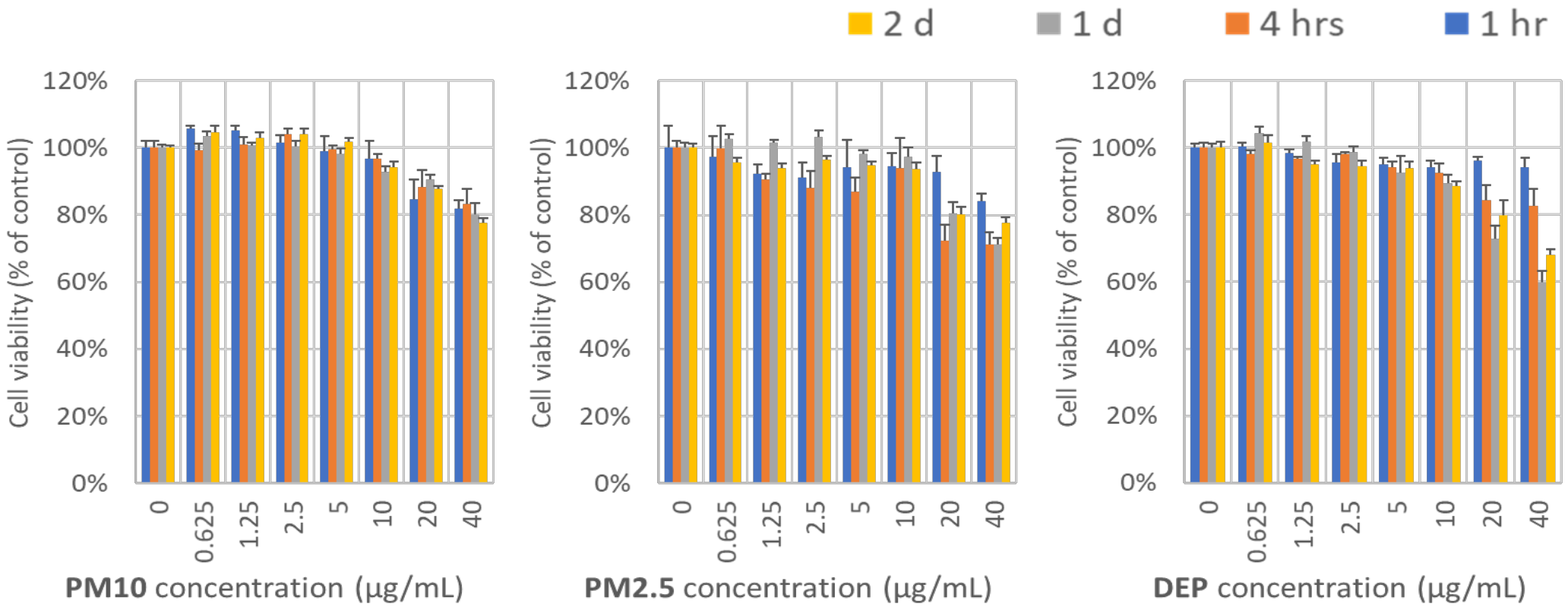


Figure 1. *Cell viability of hCMEC/D3 cells after exposure to different particles.*

Access facilities at CLF

- **Using focused ion beam scanning electron microscopy (FIB-SEM) in correlation with confocal microscopy to observe particles directly at Blood-brain-barrier (BBB)**

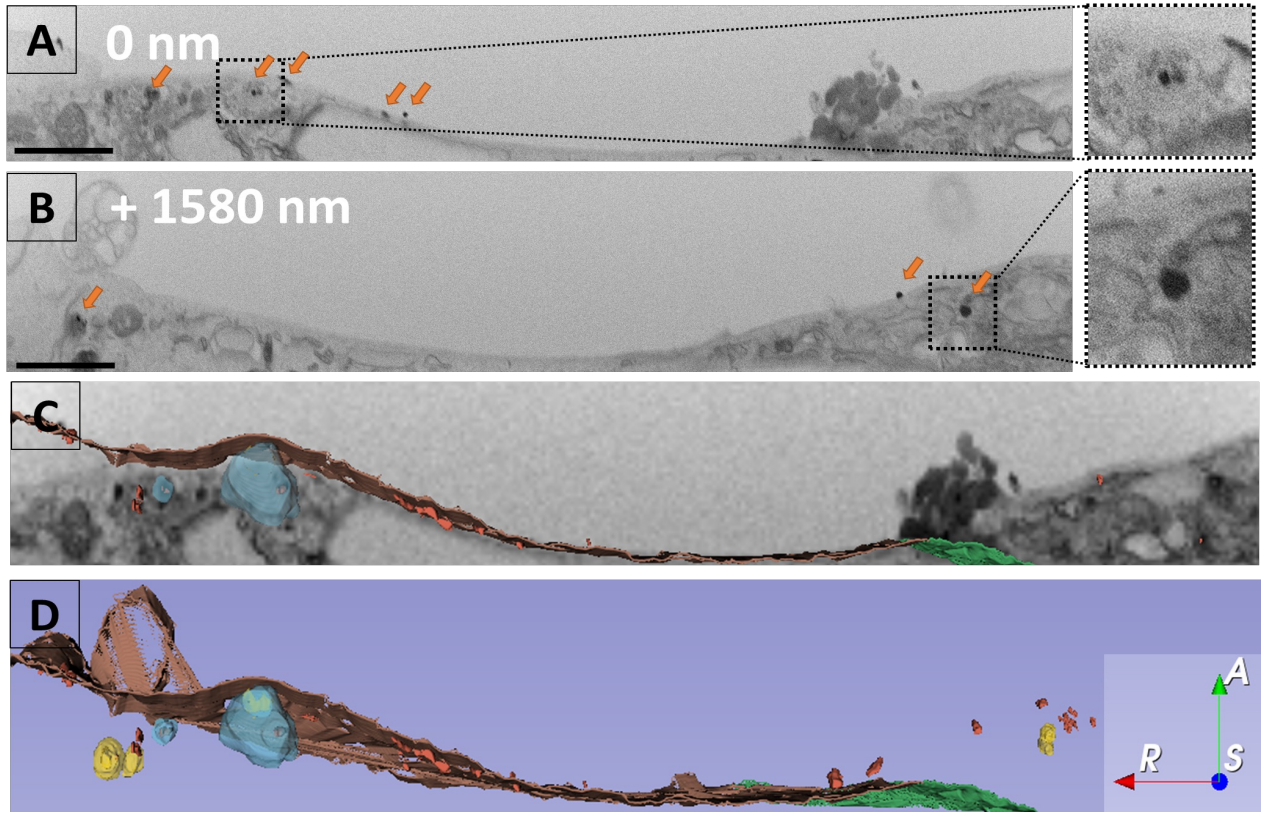


***Figure 2**. (A-B) Selected FIB-SEM images of hCMEC/D3 cells exposed to fine particles with a diameter of 2.5 µm or less (PM2.5).*

Access facilities at ISIS Neutron and Muon Source

- **Using Neutron spectroscopy to identify the lipid dynamics after exposed to particles**

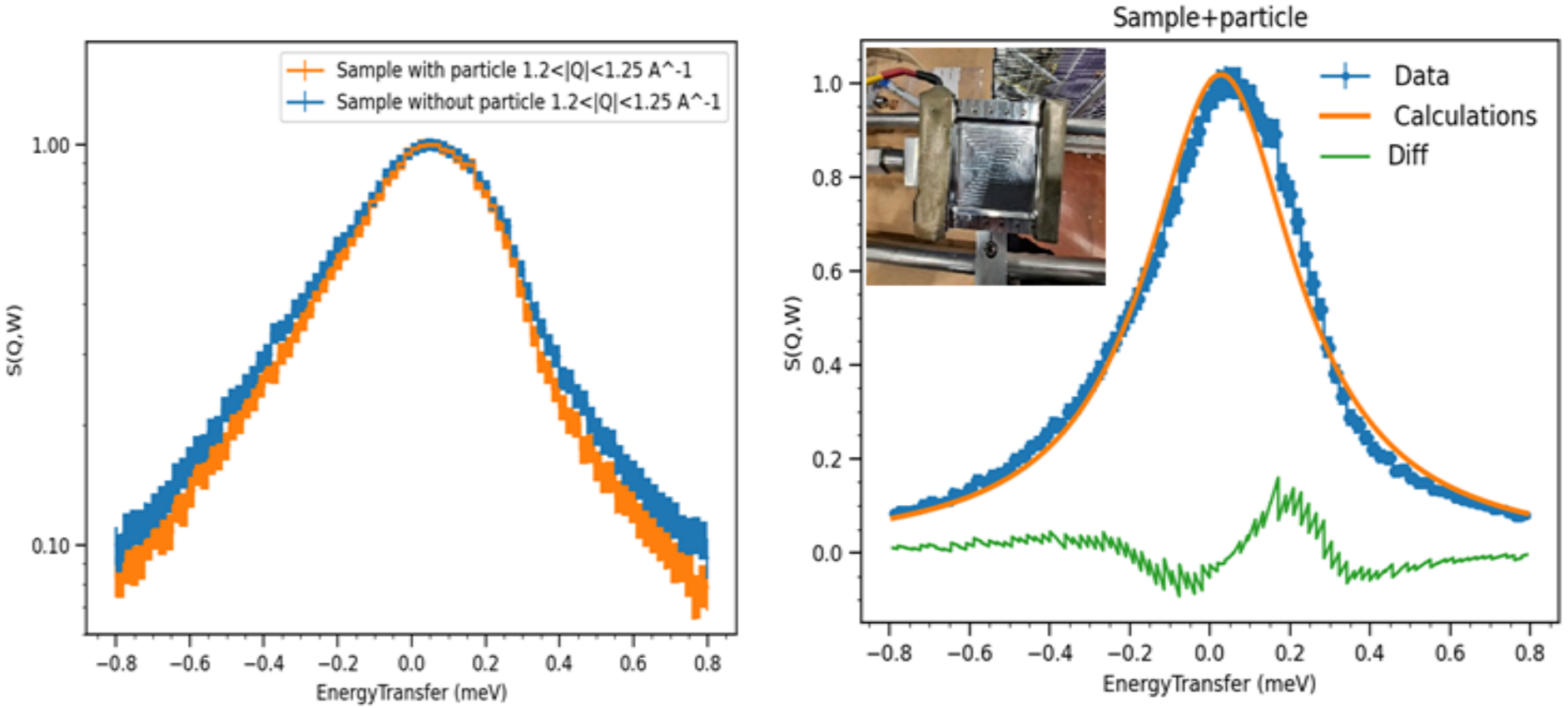


***Figure 3**. (Left) QENS spectra obtained from LET Xpress run showing decrease in lipid dynamics due to presence of particles. (Right)*

CONCLUSION / OUTCOME

- Combining a range of cutting-edge techniques through accessing the facilities at STFC, especially FIB-SEM in correlation with confocal microscopy, and neutron spectroscopy, allows us to understand more in depth how exogenous particles may egress the brain on the molecular and cellular levels.

- Further resource has been obtained to continue this work:

✓ A UKHSA PhD studentship, titled “How Might Air Pollution Hurt the Brain? – Understanding the Impacts of Inhaled Particulate Matter on Neurological Health”.

✓ BBSRC STFC facility access fund for bioscience partnerships, “Development of a novel workflow for the efficient volume imaging of thick tissue samples with correlative light and electron microscopy”.