BTS Summer Vacation Scholarship
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Characterisation of brake abrasion dust induced mitotoxicity

Brake abrasion dust (BAD) from automobiles has received little attention within the field of pulmonary toxicology although it is an environmentally abundant air pollutant which contributes up to 50 % of traffic-related particulate matter (PM). In macrophages it induces pro-inflammatory signalling and impaired pathogen clearance in a metal-dependent manner. Cationic metals accumulate preferentially in the mitochondria and are hypothesized to contribute to ambient PM-induced alterations in mitochondrial gene expression, ROS production and ultrastructure. The impact that metal-enriched BAD specifically, has on mitochondrial structure and function however, remains uncharacterized.

My summer scholarship from the British Toxicology Society at the MRC Toxicology unit Cambridge sought to characterize these damages to murine macrophages (RAW 264.7) via transmission electron microscope (TEM), branched chain amino acid assay (BCAA assay) and ultra-performance liquid chromatography mass spectrometry (UPLC-MS/MS). Our data demonstrates that sub-cytotoxic concentrations of BAD impair key mitochondrial energy metabolism pathways (UPLC-MS/MS), potentially in a metal-dependent manner. Additionally, ultrastructural changes inside the mitochondria occurred presenting as a loss of the cristae structure (TEM). The BCAA assay showed a significant increase in BCAA levels in BAD exposed cells which could be compensated by a metal chelator suggesting a metal dependent mechanism of action. Interestingly, the same increase of BCAA was observed in the diesel exhaust particle exposed cells, but the changes were not reversible by a metal chelator proposing a different mechanism of action for both particles. In the literature an increase in these amino acids is associated with decreased pyruvate utilization and decreased glucose oxidation, important steps for energy production inside the cell. Given that antimicrobial functions of macrophages are strongly ATP-dependent, and inhibited by BAD exposure, mitochondrial dysfunction may contribute to the high incidence of infection reported in traffic-dense areas.

During my stay at the MRC I was introduced to latest analytical methods in the field of toxicology and learnt to perform new assays which increased my repertoire of methods to answer scientific questions. Furthermore, I learnt to troubleshoot my experiments individually to adapt the experiment to its needs which improved my scientific skill immensely. Moreover, I gained a lot of knowledge about air pollution as a new area of toxicology establishing my learning in a review, which I have not done before.

At the end of my internship I had the chance to present the obtained data on a scientific conference which decreased my stage fright and boosted my confidence for presentations ongoing.

I am certain that the newly acquired techniques and research skills that I learned abroad will help me for the application and conduction of my PhD thesis. This scholarship offered me the chance to refine my knowledge of particulate toxicology whilst learning from experts within the field. I developed new professional relationships to scientists in the air pollution field, so that I am highly considering choosing my PhD in the toxicological research area.

I am very grateful for the British Toxicology Society and the guidance and support of my supervisor and mentor Dr. Liza Selley for the possibility to work on this project.