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Oxidative stress and aromatic hydrocarbon response of human bronchial epithelial cells exposed to petro- or biodiesel exhaust treated with a diesel particulate filter.

Authors: Hawley B et al.

Ref: [Toxicol Sci. 2014;141\(2\):505-14.](#)

Due to concerns about energy security and climate change, there is an increasing need for alternative energy sources and in that context, a variety of alternative fuels (i.e. biodiesel) is already being used. While the health effects from the exposure to diesel exhaust emissions have been well studied, there is very limited information on the toxicological properties of the emissions resulting from these new fuels. This study aimed to investigate the acute cellular responses of well differentiated normal human bronchial epithelial (NHBE) cells upon exposure to fresh, total exhaust from a diesel engine run with and without diesel particulate filter (DPF) and using traditional, petroleum diesel and biodiesel. The authors used an electrostatic in vitro exposure system to expose the cells (cultured at air-liquid interface for a minimum of 21 days) to diesel exhaust for duration of 5, 20 or 60 minutes. Cytotoxicity and transcripts associated with oxidative stress (HO-1) and polycyclic aromatic hydrocarbons (PAH) response (CYP1A1) were measured. Overall the study showed that although the particle emissions were greatly reduced in case of biodiesel and DPF-treated exhaust, the cellular responses were not mitigated due to such reductions. Moreover, upon exposure to DPF-treated exhaust significant increases in mRNA transcripts associated with oxidative stress and PAH response were observed.

Diesel and biodiesel exhaust particle effects on rat alveolar macrophages with in vitro exposure.

Authors: Bhavaraju L et al.

Ref: [Chemosphere. 2014;104:126-33](#)

Response of Wistar Kyoto rat alveolar macrophages (AMs) to diesel exhaust from a large diesel engine, equipped with full after-treatment technology (EGR, DOC and DPF), was studied. The objective of this study was to examine the toxicity of biodiesel blend (B20) and low sulfur petroleum diesel (PD) exhaust particles. In contrast to the previous study, in this study AMs were not directly exposed to diesel exhaust, instead particles were collected from the diesel particle filter and suspended in media at various concentrations. A dose dependent increase of inflammatory signals from AM after exposure were observed. In addition after 24 h exposure to B20 and PD gene expression of cyclooxygenase-2 (COX-2) and macrophage inflammatory protein 2 (MIP-2) increased. B20 exposure resulted in elevated prostaglandin E2 (PGE2) release at lower particle concentrations compared to PD. PGE2 release indicates an inflammatory response to recruit neutrophils and may also signal helper T cells. This data sug-

gests PGE2 release from AM is dependent on the chemical composition of the particles. Analysis of the particle composition showed only a 20% variation in regards to a few particle bound species, with the exception of Zn, a transition metal. Authors attributed the increase of Zn in B20 samples to possible oxidative stress-related mechanisms of toxicity. They suggest that independent composition analysis of B20 products and their consequential interactions with rat AM need to be conducted as a means to explain the difference in the response.

Biodiesel versus diesel exposure: enhanced pulmonary inflammation, oxidative stress, and differential morphological changes in the mouse lung.

Authors: Yanamala N et al.

Ref: [Toxicol Appl Pharmacol. 2013;272\(2\):373-83](#)

This study investigated the difference in toxicity induced by the exposure to biodiesel (BD) and diesel (D) particulate matter and presents the first broad assessment of inflammatory mediators in mouse lungs using BD and D. The results from this study reveal that biomarkers of tissue damage and inflammation were significantly elevated in lungs of mice exposed to BD particulates. Also, it was found that BD particulates caused a significant accumulation of oxidatively modified proteins and an increase in 4-hydroxynonenal. The up-regulation of inflammatory cytokines/chemokines/growth factors was reported to be higher in lungs upon BD particulate exposure. Furthermore, histological evaluation of lung sections indicated presence of lymphocytic infiltrate and impaired clearance with prolonged retention of BD particulate in pigment laden macrophages. Taken together, these results clearly indicate that combustion of biodiesel could exert more toxic effects compared to D. Authors suggested that the result for this may be higher oxygen content and the concentration of organic carbon (OC) of BD as well as higher soluble organic fraction that was previously reported to accelerate oxidative stress. In conclusion, this study indicated adverse effects induced by combustion emissions from neat BD in relation to petroleum D fuel, as characterized by enhanced recruitment of BAL inflammatory cells, increase in tissue damage and oxidative stress, and enhanced release of inflammatory mediators.

Differential injurious effects of ambient and traffic-derived particulate matter on airway epithelial cells.

Authors: Kumar RK et al.

Ref: [Respirology. 2015;20\(1\):73-9](#)

Exposure to airborne particulate matter (PM) may promote development of childhood asthma and trigger acute exacerbations of existing asthma via injury to airway epithelial cells (AEC). This study compared the effects of ambient airborne particulates and particulates primarily derived from motor vehicle emissions, on epithelial injury,

oxidative stress and the production of inflammatory and Th2-promoting cytokines. Results showed that ambient PM10 produced a significantly higher response from mouse AEC than traffic-derived particles, with regard to the level of mRNA expression and protein secretion of interleukin-6 (IL-6) and chemokine (C-X-C motif) ligand-1 (CXCL1, a mouse functional homologue of CXCL8). The increase in IL-6 mRNA expression and secretion was confirmed in human AEC. Also, CXCL1 mRNA expression and secretion was significantly higher after PM10 exposure when compared to PM2.5 exposure, which may have been related to the 20-fold higher level of iron in PM10. These results show that components other than traffic-derived PM are likely important in the inflammatory effects on AEC, and iron may have a significant role in these effects.

Enriched inorganic compounds in diesel exhaust particles induce mitogen-activated protein kinase activation, cytoskeleton instability, and cytotoxicity in human bronchial epithelial cells.

Authors: Seriani R et al.

Ref: [Exp Toxicol Pathol. 2015;67\(4\):323-9](#)

Diesel exhaust particles (DEP) are a major source of metallic content in air pollution. Research indicates that diesel metallic content can activate mitogen-activated protein kinase (MAPK) and may impair airway mucociliary clearance as well as alter pseudostratification of the ciliated epithelium. However, little is known about the effect of diesel metallic content on the cellular structure or the role played by MAPK activation in these effects. This study investigated the effects of DEP with enriched inorganics (high metallic content) on BEAS-2B cells on cell rheology (viscoelasticity), cytotoxicity and MAPK activation. The results showed that DEP with or without enriched inorganics reduced cell viability, however only DEP with enriched organics (high metallic content) altered cytoskeleton integrity and viscoelasticity through the differential activation of MAPK.

Global gene expression profiling of human bronchial epithelial cells exposed to airborne fine particulate matter collected from Wuhan, China.

Authors: Ding X et al.

Ref: [Toxicol Lett. 2014;228\(1\):25-33](#)

Many studies have shown that exposure to particulate matter less than 2.5µm in diameter (PM2.5) is associated with adverse health effects; however very little is understood about the complex mechanisms underlying these effects. This study used global gene expression profiling to identify genes and pathways that may contribute to PM2.5-induced lung toxicity in humans. Human bronchial epithelial (HBE) cells were exposed to various concentrations of PM2.5 collected from Wuhan, China. A total of 970 and 492 genes were identified as significantly

changed after exposure to 200µg/mL and 500µg/mL exposure, respectively. PM2.5 exposure induced expression of genes involved in inflammatory and immune responses, oxidative stress responses and DNA damage. The two doses triggered partially common disturbed pathways. However, the two doses had differential effects on cell cycle.

Ultrafine particle content in exhaled breath condensate in airways of asthmatic children.

Authors: Benor S et al.

Ref: [Journal of Breath Research 2015; 9\(2\): 026001.](#)

Ultrafine particles (UFP) are a major contributor to ambient air pollution. Long-term air pollution exposure is associated with increased respiratory symptoms and increased odds ratio of short term asthma exacerbations among children. The aim of this study was to examine whether exhaled UFP could be assessed by analysis of exhaled breath condensate (EBC), and whether exhaled UFP are correlated with symptomatic, functional and/or laboratory measures of airway inflammation in children. EBC was collected from 52 children between 6-18 years of age, 37 of which had asthma. This study showed that the load of exhaled UFP in EBC samples of children with asthma is correlated to wheezing, dyspnoea, breath score severity and the level of eosinophilia in induced sputum. Moreover, the UFP content in EBC levels significantly predicted severity of wheeze in a multivariate analysis model.

Air Pollution and Nonmalignant Respiratory Mortality in 16 Cohorts within the ESCAPE Project.

Authors: Dimakopoulou K et al.

Ref: [Am J Respir Crit Care Med 2014;189\(6\): 684–696](#)

Whilst the effects of particulate matter on cardiovascular mortality are well-known, the influence of exposure to air pollutants on respiratory mortality has not yet been as clearly demonstrated. This study reports data from 16 prospective cohort studies (n=307,553 participants) being performed in European countries as part of the European Study of Cohorts for Air Pollution Effects (ESCAPE) project. Ambient air pollutant levels were estimated based on the participants' addresses, and traffic proximity measures were also estimated. Mean age of subjects at recruitment ranged from 42 to 73 years. In contrast to previous studies which have shown inconsistent associations, this well-powered study found no statistically significant associations of air pollutants (including NO₂, NO_x, particulate matter, traffic proximity) with non-malignant respiratory mortality in this par-

ticular cohort. Hazard ratios for risk of respiratory mortality were close to 1, with little heterogeneity in results. It should be noted that ozone concentrations were not studied. Although this study did not find significant associations, it was noted that the subjects were relatively younger than subjects who may have respiratory mortality, so future studies should ideally include older subjects who may conceivably have increased respiratory mortality with air pollution.

Long-Term Effects of Traffic Particles on Lung Function Decline in the Elderly.

Authors: Lepeule J et al.

Ref: [Am J Respir Crit Care Med 2014; 190\(5\):542–548](#)

The effects of exposure to air pollutants on lung function decline is not yet well-defined in older populations. This study investigated 858 males in the Normative Aging Study cohort, a large longitudinal study of elderly subjects followed for some decades. A land use regression model was used for traffic particles (black carbon) in the greater Boston metropolitan area. Participants were studied every 3 to 5 years, including lung function test measurements. Mean age was 70 years at the first visit. The investigators found that a 0.5 $\mu\text{g}/\text{m}^3$ increase in exposure to black carbon levels was linked with an additional rate of lung function decline in FEV1 of up to 0.8% per year and in FVC of up to 0.9% per year. Furthermore, prior exposure to higher levels of carbon black in the 5 years prior was associated with lower baseline lung function at recruitment. These associations occurred in exposures levels that generally did not exceed air quality standards. Overall, this study demonstrated the long-term effects of traffic particles on the rate of lung function decline in older people, who would be considered to be more vulnerable to air pollutants.

The Cost of Air Pollution: Health Impacts of Road Transport.

Authors: OECD (2014),

Ref: OECD Publishing. <http://dx.doi.org/10.1787/9789264210448-en>

The World Health Organization has estimated that 3.7 million people died globally because of outdoor air pollution in 2012. The OECD has now estimated the economic costs of air pollution from road transport, through calculating the financial implications to society of the health impacts of exposure to traffic-related pollutants. Methods used in the report were linking of sector-specific evidence of exposures from road transport emissions, epidemiological evidence of health effects, and economic evidence of costs of health impacts. The report estimated that, in OECD countries, the cost of the health impact of outdoor air pollution, in relation to mortality and mor-

bidity, was approximately USD 1.7 trillion in 2010, with road transport air pollutant exposure accounting for approximately 50% of this cost. Estimates for China and India, also included in the report, were also substantial. Given the size of these economic costs, the OECD report recommended that governments continue to exercise public health policy, including strict vehicle regulation standards, and regulatory approaches in public transport in general, to aim to reduce traffic-related emissions.

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