3545 Particulate Matter Exposure Alters the Luminal and Mucosal Gut Microbiome of ApoE-/- and Ldlr-/- Mice

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There is a strong body of literature demonstrating the adverse effects of ambient air pollution exposure on human health. Air pollution-related deaths have been primarily attributed to cardiovascular (CV) diseases. Ambient ultrafine particles (UFP) produced by traffic emissions induce pro-oxidative effects in the blood and alter plasma lipoproteins. While almost weightless, UFP represent 85-90% of PM2.5, display biophysical and biochemical properties that lend to their increased toxicity, and thus promote atherosclerosis to a greater degree than pollution particles of a larger size. The gastrointestinal (GI) tract may be exposed to UFP as rapid bronchial mucocilliary clearance transports the inhaled particles to the oropharynx, followed by swallowing. When the UFP reach the GI tract, they can influence the gut microbiome, which has been shown to be a critical mediator in maintaining gut health and plays an important role in the development of cancer, metabolic, and CV diseases. Dysbiosis (altered composition and reduced diversity of the microbiome) modulates host metabolism, immunity, and inflammatory responses, leading to pathogenesis. I hypothesize that UFP promote dysbiosis of the gut microbiome in metabolic mouse models ApoE-/- and Ldlr-/-. Male 8 week old ApoE-/- mice and 10 week old Ldlr-/- mice were exposed to particulate matter, 3 times a week by gavage of 30µg/mouse. 16S rRNA gene sequencing was performed to characterize gut microbiome diversity and composition of the luminal and mucosal jejunum and cecum. The luminal microbiome of Ldlr-/- mice exposed to PM showed a statistically significant reduction ($p<0.05$) in alpha diversity by the Shannon index (reflecting species richness and evenness) as well as significant ($p<0.001$) changes in beta diversity (reflecting a difference in overall microbial composition). The luminal microbiome of ApoE-/- mice exposed to UFP also showed significant ($p<0.05$) changes in beta diversity. The taxonomic changes in the microbiome speak to the varied toxicological response of two different hyperlipidemic mouse models to air pollution particulates, supporting the necessity to further investigate the effects of UFP on the gut microbiome as an environmental trigger of disease.

3546 Modeling the Load of SARS-CoV-2 Virus in Human-Expelled Particles during Coughing and Speaking

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Indoor environments are ideal spaces for airborne transmission of pathogens due to the favorable relative humidity (RH) and temperature levels, as well as the absence of ultraviolet radiation. These pathogens can also generate endotoxins, leading to respiratory effects to exposed populations. The load and viability of indoor bioaerosols transported under various environmental conditions complicate our understanding of risks associated with indoor bioaerosols. However, the evolution of pathogen-containing droplets and the size-dependent pathogen load have not been studied in detail. The lack of this information leads to uncertainties in understanding the airborne transmission of respiratory diseases, such as the COVID-19. In this study, through a set of differential equations describing the evolution of respiratory droplets and by using the SARS-CoV-2 virus as an example, we investigated the distribution of airborne virus in human expelled particles from coughing and speaking. More specifically, by calculating the vertical distances traveled by the respiratory droplets, we examined the number of viruses that can remain airborne and the size of particles carrying these airborne viruses after different elapsed times. From a single cough, a person with a high viral load in respiratory fluid (2.35×10^9 copies per ml) may generate as many as 1.23×10^5 copies of viruses that can remain airborne after 10 seconds, compared to 386 copies of a normal patient (7.00×10^6 copies per ml). Masking, however, can effectively block around 94% of the viruses that may otherwise remain airborne after 10 seconds. Our study suggests that in general, particles above 100 µm can settle down to the ground within a few seconds and those smaller can remain airborne for a sufficient longer period of time. The results from this study challenge the conventional understanding of disease transmission routes through airborne and droplet mechanisms, which are separated by a size boundary of 5 µm. We suggest that a complete understanding of the respiratory droplet evolution is essential and needed to identify the transmission mechanisms of respiratory diseases.

3547 Evaluation of Pulmonary Effects of 3D Printer Emissions from Acrylonitrile Butadiene Styrene Using an Air-Liquid Interface Model of Primary Normal Human-Derived Bronchial Epithelial Cells

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This study investigated the inhalation toxicity of the emissions from 3-D printing with acrylonitrile butadiene styrene (ABS) filament using an air-liquid interface (ALI) *in vitro* model. Primary normal human-derived bronchial epithelial cells (NHBEs) were exposed to ABS filament emission particles in an ALI for 4 h. The mean and mode diameters of ABS emitted particles in the medium were 175 ± 24 nm and 153 ± 15 nm, respectively. The average particle deposition per surface area of the epithelium was $2.29 \times 10^7 \pm 1.47 \times 10^7$ particle/cm^2, equivalent to an estimated average particle mass of 0.144 ± 0.042 µg/cm^2. Results showed exposure of NHBEs to ABS emissions did not significantly affect epithelium integrity, ciliation, mucus production, nor induce cytotoxicity. At 24 h after the exposure, significant increases in the pro-inflammatory markers IL-12p70, IFN-γ, TNF-α, IL-17A, VEGF, and MIP-1α were noted in the basolateral cell culture medium of ABS-exposed cells compared to non-exposed chamber control cells. Results obtained from this study correspond with those from our previous *in vivo* studies, indicating that the increase in inflammatory mediators occur without associated membrane damage. Furthermore, the combination of the exposure chamber and the ALI-based model is promising for assessing 3-D printer emission-induced toxicity.

3548 Immunotoxicity Prediction on Chemical Substances through Profiling of Cytokines Production from THP-1 Cell Line

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Alternative test method for screening immunotoxic substances has not been actively challenged and no test guideline has been officialized internationally. We developed an alternative method for screening immunotoxic substances through profiling cytokines production from THP-1 dendritic cell line (IMMUNOTOX-T) considering antigen presenting cell as a major cell involved with immune modulation. Seven immunosuppressants, 15 non-immunotoxicants, and 41 substances with immunotoxicity potentials based on *in vivo* data were used. Following 24h stabilization period, those substances were added as concentrations of 0.01x, 0.1x, 0.5x 75% cell viability, which was decided by CCK assay, in the presence of LPS stimulant. Cell culture supernatants were collected at 24h after stimulation, and profiling of 24 cytokines production were examined using a Luminex system. The relative cytokine production levels (RCPL,% versus vehicle control) were calculated for each individual cytokine at each concentration of test substance. Then, the acceptable cytokine production ranges (ACPR) were established for reflecting lowest to highest RCPL for all 15 non-immunotoxicants. Furthermore, the mean cytokine production values (MCPVS) were defined to grand average of RCPL for the 7 immunotoxicants. Prediction of immunotoxicity potential (PIP) was set up through adopting combinatory algorithm of those parameters. If mean RCPL of 3 test concentrations was below MCPVS, the substance was defined as downregulatory and if mean RCPL was higher than highest ACPR of non-immunotoxicants, the substance was defined as upregulatory for the that cytokine. PIP was obtained for 40 substances (97.6%). Considering down- or -up regulatory judgements for all 24 cytokines together, if over 70% were on downregulatory, the substance was categorized into suppressor (14 substances), and vice versa for upregulatory, 12 substances were categorized into enhancer, and 14 borderline substances with no over 70% available. The IMMUNOTOX-T assay method suggests THP-1 cell line as a valuable cell to develop *in vitro* method for immunotoxicity. *Supported by grant # 20183MFDS524, Ministry of Food and Drug Safety and by the Ministry of Environment-Educational training program for the management of information on the hazards and risk of chemical substances.*

3549 Lack of Biological Activity of Benzoic Acid, Its Salts, and Esters

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The objective of this work was to explore the biological activity of benzyl alcohol, benzoic acid, its salts (Na^+-, K^+-, Ca^{2+}-, Mg^{2+}- and $NH4^+$-benzoate), and esters (methyl-, ethyl-, butyl- and propyl-benzoate) to define biological similarity as support for a read across approach for risk assessment for this class of preservatives. The comprehensive transcriptional response of MCF7, A549, HepG2 cells and cardiomyocytes was evaluated (TempO-Seq) after exposure to vehicle-control or each of the benzoates (at 1, 100, or 500 µM), for 6h. Our results show that very few chemicals of the group elicited a significant transcriptional response (FDR<0.05, fold change >1.2) in any of the 4 cell lines evaluated. Only Ca^{2+}-benzoate, propyl benzoate and

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