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| **Bushfire-derived particulates impairs epithelial cilia activity, ion transport and innate immunity** |
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| **Introduction:** Inhalation of bushfire particulates impairs lung health and contributes to chronic respiratory disease exacerbations. It is critical to develop appropriate models to investigate the impacts of bushfire particulate matter, understand the underlying mechanisms and develop effective interventions.**Aim:**1. To assess the effects of bushfire particulates on physiological and immune functions in peripheral bronchial epithelial cells (pBECs) from healthy individuals and patients with chronic respiratory diseases.

**Methods:** Representative flora (NSW, Australia) was combusted and particulates mechanically sorted by size (PM1, PM2.5, PM10). ALI cultures of pBECs from healthy subjects and patients with asthma or chronic obstructive pulmonary disease (COPD) were exposed to particulates (0.45µg/cm2, 7 days) using a custom-designed chamber and dry powder nebuliser (ElectroMedical Measurement Systems, UK). A subset of cells were subsequently infected with rhinovirus A1 (RV-A1). Ciliary function was assessed by high-speed video recordings (CiliaFA plugin; ImageJ), and transepithelial sodium and chloride ion transport quantified using an Ussing chamber (Physiologic Instruments, USA). Cytokines and toll-like receptors (TLRs) were quantified by qPCR and ELISA. **Results:** Cilia beat frequency in pBECs from healthy subjects was impaired by PM1, PM2.5, and PM10 (10.4±1.1 (SEM); 10.0±1.1 and 8.7±0.8 vs. 11.6±1.1 Hz in control; n=7, p<0.05). Sodium channel, cystic fibrosis transmembrane conductance regulator (CFTR), and calcium-dependent ion transport was impaired by PM2.5 and PM10 (5.9±1.0 and 4.5±0.9 vs. 8.9±1.6 μA/cm2 in control; p<0.05).Similar results were observed from patients with asthma or COPD, although baseline CFTR function (5.7±0.38 μA/cm2; p<0.05) and cilia active area was lower in COPD. Particulates reduced IL-6 and IL-8 responses and TLR expression in pBECS from asthmatic patients, and altered responses to RV-A1 infection.**Conclusion:** Bushfire particulatematter impaired cilia function and CFTR-mediated chloride secretion in pBECs from healthy subjects and patients with chronic respiratory diseases, and reduced inflammatory cytokines in pBECs from asthmatic patients.**Grant Support:** Medical Research Future Fund, Rainbow Foundation |