| Author | Air pollutant | Material/subjects | Country | Mechanism | Main results |
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| Becker and Soukup 1999 [84] | NO2 (different concentrations: 0.5, 1.0, and 1.5 ppm) | Human bronchial epithelial cell line BEAS-2B | USA | Viral replication<br>IL- 6, IL-8 | RSV internalization increased by 0.5 ppm exposure and decreased by 1.5 ppm exposure;<br>The release of infectious virus 48 h postexposure was reduced only after 1.5 ppm NO2 exposure;<br>Reduced IL-6, IL-8 |
| Becker, Soukup 1999 "Exposure to urban air particulates alters…" [67] | PM10 (EHC-93) | human bronchial epithelial cell line BEAS-2B subclone S6 and human alveolar macrophage from BAL from volunteers | USA | Viral uptake<br>IL-8, MIP-1alpha, MIP-1beta, MCP-1, RANTES | 50% decrease in viral uptake of virus by AM;<br>MCP-1 production inhibited;<br>MIP-1 and IL-8 levels lower than expected from a combined response; |

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| | | | | | RSV-induced production of RANTES by epithelial cells was decreased in the presence of AM, but not affected by PM10 |
| Castro 2008 [91] | Cigarette smoke condensate | A549, human alveolar type II–like epithelial cells, and 293, a human embryonic kidney epithelial cell line | USA | IL-8 (gene and protein expression), MCP-1 (gene and protein expression), nuclear factor kappa B (NF-kB) | Increased IL-8 and MCP-1 gene and protein expression Enhanced activation of interferon regulatory factor (IRF)-1 and IRF-7 Enhanced activation of NF-kB, and increased NF-kB–driven gene transcription. Increased chemokine expression in airway epithelial cells |

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| Castro 2011 [72] | cigarette smoke extract | Human plasmacytoid dendritic cells | USA | IFN-$\alpha$<br>IL-1$\beta$, IL-6, IL-10, TNF-$\alpha$, CCL2 (MCP-1), CCL3 (MIP-1a), CCL5 (RANTES), CXCL10 (IP-10), CXCL8 (IL-8)<br><br>qRT-PCR for IRF-7, TLR7, TLR9 and 18S<br>Intracellular staining of IRF-7 | Inhibited RSV-induced IFN-$\alpha$ in pDC, inhibited release of IL-1$\beta$, IL-10 and CXCL10.<br>Not altered: IL-6, TNF-$\alpha$, CCL2, CCL3, CCL5 and CXCL8<br>Decreased the expression of toll-like receptor (TLR)-7 and interferon regulatory factor (IRF)-7 in RSV-infected pDC.<br>CSE prevented IRF-7 activation. |
| Chakraborty 2017 [42] | TiO2-NP | Human primary bronchial epithelial cells) | USA | Expression of NGF and its receptors: TrkA and p75NTR<br>Autophagy (beclin-1 expression)<br>Cell death (FACS after annexin V/propidium iodide staining) | RSV infection efficiency more than doubled;<br>NGF and its TrkA receptor upregulated;<br>Silencing NGF gene expression with siRNA significantly |

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| | | | | | inhibited RSV infection; Increase in necrotic cell death and reduction in apoptosis; Increase in expression of the autophagosomal gene beclin-1; Pharmacological inhibition of beclin-1-> increased apoptotic rate and lower viral load |
| Cruz-Sanchez 2013 [43] | Mimics of ambient particulate matter ($PM_{10}$) | human epithelial-2 (HEp-2) cells 1HAEo-cells-normal human airway epithelial cells transformed with Simian virus 40 | Canada | IL-6, IL-8 RSV survival | Increased IL-6 and IL-8 Accelerated viral entry (the mechanism involved endocytic pathway; dynamin dependent) |
| Foronjy 2014 [86] | Cigarette smoke | C57BL/6J mice (repeated RSV | USA | Histological analysis | Enhanced influx of macrophages, |

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| | | exposition- 6 times) | | Protease and Cytokine Measurements Intracellular Signaling (cathepsin E, S, G, K, W, Z, MMP-28, actin) Terminal Deoxynucleotidyl Transferase dUTP Nick Endlabeling (TUNEL) Analysis Viral titers Phosphatase Levels (PP2A and PTP1B) | neutrophils and lymphocytes; Most pronounced around the vasculature and bronchial airways; Airspace enlargement and fibrosis; Induced cytokine (IL-1$\alpha$, IL-17, IFN-$\gamma$, KC, IL-13, CXCL9, RANTES, MIF and GM-CSF) and protease (MMP-2, -8, -12, -13, -16 and cathepsins E, S, W and Z) expression.; Enhanced apoptosis; Reduced protein phosphatase 2A (PP2A) and protein tyrosine phosphates |

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| | | | | | (PTP1B) expression and activity |
| Foronjy 2016 [87] | Cigarette smoke | lung BALF from age-matched healthy control subjects, smokers, and subjects with COPD<br><br>Ptp1b (Ptpn1 gene) knockout (-/-) mice<br><br>human primary small airway epithelial and mouse bone marrow derived macrophages | USA | Protein tyrosine phosphatase 1B (PTP1B)<br><br>S100A9<br><br>Caspase-3, p-IκBα, IκBα (Ser32), p-p38 (Thr180/Tyr182), p38, TRIF, MyD88, IRAK1, pp44/42 MAPK (Erk1/2) (Thr202/Tyr204), ERK1/2, β-actin<br><br>Viral titer | Ptp1b -/- mice -> exaggerated immune cell infiltration, damaged epithelial cell barriers, cytokine production, increased apoptosis, and elevated expression of S100A9<br>Pre-exposure to cigarette smoke desensitized PTP1B activity -> enhanced S100A9 secretion and inflammation.<br>S100A9 levels in human BALF- an inverse relationship with lung function in healthy subjects, |

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| | | | | | smokers and COPD subjects. HBEC from COPD donors-secreted more S100A9 following RSV infection. |
| Groskreutz 2009 [44] | Cigarette smoke extract | Primary human tracheobronchial epithelial | USA | Cytokine measurements<br>Cell Death Detection (ELISA + TUNEL Assay)<br>Cell Survival Assays<br>Fluorescent RSV/DAPI Staining<br>Plaque Assay<br>Western blot detection of cleaved caspases 3 and 7 showed | Less apoptosis;<br>Necrosis rather than apoptosis;<br>Less live cells, but increased viral load;<br>The effect inhibited by pretreatment with N-acetylcysteine and aldehyde dehydrogenase;<br>Cigarette Smoke Prevents RSV- and Staurosporine-Induced Caspase 3 and 7 Activation;<br>p53 or XIAP not altered |

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| Harrod 2003 [29] | Diesel engine emissions | C57Bl/6 mice | USA | Inflammatory cells in BALF<br><br>Lung histology<br><br>TNF-$\alpha$, IFN-$\gamma$<br><br>Clara cell secretory protein, CCSP (=CC-10 or CC-16)<br><br>Surfactant protein A (SP-A) and proprotein B (proSP-B) | Increased viral gene expression; Increased cell numbers in BALF, domination of alveolar macrophages (AM, >95%); Augmented lung inflammation (peribronchial and peribronchiolar regions) and airway epithelial remodeling (loss of the normal cuboidal appearance of nonciliated bronchiolar epithelial (Clara) cells; increased appearance of pseudostratified, columnar epithelial cell morphology and apparent airway |

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| | | | | | epithelial cell sloughing); a dose-related increase in lung histolopathology; Mucous cell metaplasia; Increased TNF-$\alpha$and IFN-$\gamma$; Attenuation of CCSP production, the numbers of CCSP-producing cells diminished; Surfactant proprotein B (proSP-B) decreased; Decreased SP-A |
| Hashiguchi [85] | TiO2-NP | BALB/c mice | Japan | IL-2, IL-4, IL-10, IFN-$\gamma$, RANTES (CCL5), MIP-1$\alpha$ (CCL3)<br>Flow cytometric analysis<br>Histological examination<br>Viral titres | Increased IFN-$\gamma$and RANTES<br>Viral titers unaffected<br>An increase in the infiltration of lymphocytes into the alveolar septa in lung tissues |

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| Hirota 2015 [73] | PM10 (EHC93) | human airway epithelial cell line (HBEC-6KT) | Canada | IL-1β, CCL20, GM-CSF, TSLP, IL-33, and IL-25<br>Differential Interference Contrast and Scanning Confocal Microscopy | No effect on IL-1β responses |
| Hobson and Everard 2007 [48] | Nitric oxide | human monocyte-derived dendritic cells (DCs) | UK | Viral titres<br>Viral persistence | RSV replication outside the RSV epidemic season after exposure to nitric oxide |
| Ivanciuc 2019 [112] | side-stream tobacco smoke | cystathionine γ-lyase enzyme (CSE)- deficient and wild-type mice | USA | Aairway hyperresponsiveness (AHR) to methacholine challenge<br>Viral replication<br>Inflammatory cytokines and chemokines | CSE-deficient mice: more severe clinical disease, airway obstruction and AHR, enhanced viral replication and lung inflammation, a significant increase in the number of neutrophils in BALF, increased |

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| | | | | | levels of inflammatory cytokines and chemokines. |
| Kaan and Hegele 2003 [47] | PM10 (EHC-93) | Guinea pig alveolar macrophages | Canada | IL-6, IL-8<br>RSV Yield (the amount of viral replication per RSV-immunopositive cell) | Enhanced secretion of TNF-$\alpha$, decreased RSV Yield |
| Lambert 2003 "Effect of Preexposure to Ultrafine Carbon Black…" [79] | Preexposure to ultrafine carbon black | BALB/c mice | USA | TNF-$\alpha$<br>IL-13<br>IFN-$\gamma$-inducible protein 10 (IP-10) mRNA<br><br>lymphotactin, RANTES, eotaxin, MIP-1$\alpha$, MIP-1$\beta$, MIP-2, MCP-1, and TCA-3, housekeeping genes L32 and GAPDH<br><br>RNA templates for interleukins 10, 13, 15, 9, 2, 6, and IFN-$\gamma$and interleukins 10, 1$\alpha$, 1$\beta$, 1R$\alpha$, 6, | Reduced TNF-$\alpha$in BALF on days 1 and 2 of infection; a reduction in BALF lymphocyte numbers on day 4, reduced IP-10, lymphotactin, and IFN-$\gamma$ mRNAs;<br>No changes in RANTES, eotaxin, MCP-1, MIP-1;<br>Lower viral titers on days 2– 4 of infection; by day |

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| | | | | and IFN-γ, L32 and GAPDH genes | 7 neutrophil numbers, proinflammatory cytokine mRNA expression, and protein levels of TNF-αand IL-13 increased |
| Lambert 2003 "Ultrafine Carbon Black Particles Enhance…"[96] | Ultrafine carbon black after RSV infection | BALB/c mice | USA | AHR to methacholine<br><br>bronchoalveolar lavage and cell differentials<br><br>MIP-1α, MCP-1, and RANTES<br><br>RSV antigen quantitation<br><br>Laser capture microdissection of alveolar epithelium<br><br>Reverse transcription (MIP- | Viral titer and clearance unaffected by CB exposure; Neutrophil numbers elevated on days 4 and 7, and lymphocyte numbers were higher on days 4 and 14 of infection in CB-exposed, RSV-infected mice; Enhanced AHR, BAL total protein, MCP-1, |

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| | | | | 1α and the housekeeping gene L32) | MIP1-α, RANTES; MIP-1-α mRNA expression increased in the alveolar epithelium, where ultrafine particles deposit in the lung |
| Mebratu 2016 [78] | Cigarette smoke | C57BL/6 mice | USA | Lung inflammatory cells, histology and morphometry<br><br>TUNEL assay<br><br>mRNA levels for IL-17a, IL-17c, IL-17d, IL-17 f. IL-1β, IL-12b, IL-18, IL-23a, Ccl-2, Ccl-7 at day 4 post infection in lung tissue<br><br>Quantitative RT-PCR for MMP-12 mRNA at day 14 post infection.<br><br>Viral load | Inflammation characterized y by lymphocytes and neutrophils; Robust emphysema with enhanced MMP-12 mRNA expression and TUNEL positivity; Increased the levels of IL-17 (a, b, d, f), IL-1β, IL-12b, IL-18, IL-23a, Ccl-2, Ccl-7 mRNAs in the lungs; By day 4 lower copy number of |

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| | | | | | viruses, but higher on day 14. |
| Modestou 2010 [45] | Cigarette smoke extract | Human trachea and bronchial samples<br><br>Primary human tracheobronchial epithelial cells | USA | Antibodies against:<br>- interferon regulatory factor-9 (IRF-9)<br>- ICAM-1<br>- Stat1<br>- tyrosine-701 phosphorylated human Stat1<br>- heat shock protein (HSP)-90<br>- β-actin<br>- serine-727 phosphorylated human Stat1<br>- serine-727 phosphorylated human Stat1<br>ICAM-1<br>Epithelial Cytotoxicity Assays<br>Glutathione Assay | Inhibited IFN-γ-dependent gene expression (not due to cell loss or cytotoxicity); Inhibited IFN-γ-induced Stat1 phosphorylation; Decreased inhibitory effect of IFN-γ on RSV mRNA and protein expression; CSE effects on IFN-γ-induced Stat1 activation, antiviral protein expression, and inhibition of RSV infection decreased by glutathione augmentation of epithelial cells (N-ACC or glutathione monoethyl ester) |

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| Phaybouth 2006 [46] | side-stream cigarette smoke | Newborn BALB/cmice (RSV infection twice) | USA | Pathologic analysis<br>RT-PCR analysis of viral gene expression<br>IL-5, IL-12, IL-13, and IFN-γ<br>CCSP | Neutrophilia and decreased CCSP levels in response to RSV rechallenge;<br>An increase in BALF eosinophils, reduced levels of IFN-γ, and IL-12, decreased lung tissue inflammation, and decreased mucus production after RSV rechallenge;<br>Increased viral gene expression |
| Poon 2019 [111] | Cigarette smoke- mice<br><br>COPD patients<br>Smokers | Mice exposed to cigarette smoke<br><br>BALF from healthy never smokers, smokers, and COPD patients | USA | LIF<br>LIFR | LIF in human BALF reduced in both smokers and COPD patients;<br>HBE cells isolated from COPD patients produced less LIF during RSV infection; |

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| | | Human bronchial epithelial (HBE) | | | Reduced LIF and its receptor (LIFR) in mice lungs Smoke-exposed animals had reduced LIF expression during RSV infection. |
| Smallcombe 2020 [37] | Titanium dioxide nanoparticles | Immortalized human bronchial epithelial cells<br><br>C57BL/6 mice | USA | Epithelial cell barrier integrity<br>Viral titer<br>Reactive oxygen species (ROS) generation | Apical junctional complex (AJC) disruption induced by RSV amplified by TiO2-NP;<br>Increased viral infection in epithelial cells;<br>TiO2 induced generation of ROS, and pretreatment with antioxidant (N-ACC) reversed barrier dysfunction;<br>In vivo, RSV-induced injury and AJC disruption were |

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| | | | | | augmented in the lungs of mice given TiO2-NP; Airway inflammation was exacerbated (WBC infiltration into the BAL), along with exaggeration of peribronchial inflammation and AJC disruption |
| Raza 1999 [77] | water-soluble cigarette smoke extract (CSE), nicotine, cotinine | monocytes of the blood from donors | UK | TNF-$\alpha$<br>nitric oxide (NO)(as nitrites) | Increased TNF-$\alpha$ and decreased NO, higher proportion of extreme responses |
| Soukup, Koren, Becker 1993 [83] | ozone | Human alveolar macrophages | USA | IL1, IL-6, TNF<br><br>Percentage RSV-infected AM<br><br>Amount of infectious virus released | No difference in percentage of infected AM or in the amount of infectious RSV produced; Effects on IL-1 and Il-6 secretion were only found with the lowest |

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| | | | | | levels of infection which induced cytokine release;<br>TNF production unaffected by ozone |
| Urrego 2009 [98] | Nicotine exposure | Rats | USA | RT-PCR for NGF, brain-derived neurotrophic factor (BDNF), p75NTR, trkA, trkB, and the housekeeping gene β-actin<br><br>NGF, BDNF, p75NTR, trkA, trkB, protein levels<br><br>Extravasation of albumin from airway blood vessels. | An additive effect on NGF expression, exaggerated neurogenic airway inflammation (abolished by selective inhibition) |

**Table S2**. The characteristics of the studies included in the scoping review.