Particulate matter-induced oxidative stress – recent mechanistic insights from in vitro studies

Vânia Vilas-Boas, Nivedita Chatterjee, Andreia Carvalho, Ernesto Alfaro-Moreno

Nanosafety Group, International Iberian Nanotechnology Laboratory, Braga, Portugal.

\*Corresponding author: [vania.vilasboas@inl.int](mailto:vania.vilasboas@inl.int)

**Table S1 –** Main oxidative stress-related effects triggered by particulate matter reported in the latest in vitro lung studies and tested antioxidant strategies. Cited papers were available on Pubmed on 13.07.2023 and published after 2020.01.01.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Cells/cell line** | **Type of PM, conc., time of exposure, condition** | **Observed effects** | **Treatments & other observations** | **Reference** |
| A549 | CSE, 3 and 6%, 12h, SUB | ↑ LC3B-II, protein carbonylation, translocation of ADAR1 from nucleus to cytosol  ↓ ADAR1 (but not mRNA, so it’s post-transcriptional), *CYP1A1*, RNA editing levels of AhR, SOD act. | Similar effects were induced by acrolein but not by nicotine. Decreased ADAR1 by CSE were mediated by autophagy. Authors hypothesize such translocation is mediated by the MAPK/ERK pathway, as CSE has been previously reported as an MAPK3 (ERK1) and MAPK8 (JNK1) activator. | (Takizawa et al., 2020) |
| A549 | Comercial CSE, 0.25 & 1μg/mL, 24h, SUB | ↑ IL-6, IL-8, MCP-1, CCL5, CYBA, SOD, GPx, CAT, NOX, Nrf2, ATG5, ATG12, ATG16, beclin-1, LC3B-II/LC3B-I, autophagosome formation, FOXO1, nuclear FOXO3a  ↓ FOXO3a, mTOR  No change in cell viability, ANXV+ or Pi+ cells (= no necrosis, no apoptosis) | Pre-treatment w/ 1mM **NAC** for 2h decreased mRNA expression of cytokines, chemokines, and autophagy-related proteins, therefore, supporting a role for ROS in the activation of CSE-induced autophagy. FOXO3a knock-down aggravated the pro-oxidative and pro-inflammatory effects, while stimulating autophagy. | (Bagam et al., 2021) |
| A549 | PM10 SRM 1648a water-soluble fraction, 400μg/mL, 24h, SUB | ↑ MDA, NO, *MEK5, ERK5*, p-ERK5, Nrf2, HO-1  ↓ cell viability, SOD act., CAT, GSH | Pre-treatment w/ **biochanin A** for 2h protected cells against WS-PM-induced oxidative stress via MEK5/ERK5/Nrf2 activation. | (Xue et al., 2021) |
| A549 | PM SRM 1648a, 25-200μg/cm2 (119-950μg/mL), 24h, SUB | ↑ ROS, p-AMPKα, Sestrin2 (oxidative stress suppressor), IL-8, TNF-α, COX-2  ↓ cell viability, mitochondrial function | 5-Aminoimidazole-4-carboxamide ribonucleoside (AICAr), an AMPK activator used to mimic exercise in vitro, restored O2 consumption rate and decreased inflammatory profile. Confirmed in mice (inhalation), the results suggested that PM derived-effects are not exacerbated, but rather alleviated, by exercise-induced hyperventilation. | (So et al., 2022) |
| A549 | PM SRM 1649b Organic extractable fraction, 100μg/mL, 24h, SUB | ↑ wound healing, cell migration, vimentin, fibronectin, ETS-1, p-p65 NF-κβ  ↓ E-cadherin | O-PMs induced EMT in a ROS dependent way. Pre-treatment with 5mM **NAC** for 1h decreased fibronectin production and EMT transition, proving their dependence on ROS generation. Confirmed in mice (intratracheal instillation). | (Chen et al., 2020) |
| A549 | PM2.5 (Water-soluble fraction in simulated lung fluid), 50-200μg/mL, 24h, SUB | ↑ LDH, DNA damage, proline expression  ↓ cell viability, TAC | Proline prevented DNA damaging effects of PM2.5.  Higher levels of metals in the urban PM2.5 (vs industrial) resulted in lower cell viability. Highlights the role of soluble metal contents in PM samples. | (Barzgar et al., 2023) |
| A549 | PM2.5 (brake-derived) w/ ≠ Cu conc., 50-500μg/mL, 48h, SUB | ↑ ROS, % apoptotic cells, MitoMP, *IL-8, IL-1α, IL-6, TNF-α, HO-1*  ↓ Cell viability, *Bcl-2* | Effects (except inflammation) correlated w/ Cu content of the samples as the PM w/ no Cu did not induce any toxicity. Authors advocate for elimination of Cu from brake pads, and suggest ROS increase as an early marker of cytotoxicity induced by metals and PM. | (Figliuzzi et al., 2020) |
| A549 | PM2.5 Urban vs industrial, 80μg/mL, 24h, SUB | ↑ ROS, TNF-α (non-pollution), IL-6 (industrial)  ↓ Cell viability, *NOQ1* | PM2.5 conc higher in urban setting and in pollution stage. Interestingly, in the pollution stage, both types of PM induced lower levels of ROS than in the non-pollution stage. TNF-α levels correlated w/ Na+ and SO24- and w/ metals (As, Cr, Cu, Fe, Mn, Ni, Ti, Sr, Zn). | (Pang et al., 2020) |
| A549 | PM2.5, 80μg/mL, 24h, SUB | ↑ ROS, IL-6, TNF-α, LDH  ↓ Cell viability (significant but not relevant) | Positive correlations were found between the toxicity indexes, particularly ROS generation, and the components of the PM2.5 such as EPFRs (eg. PAH radicals), organic carbon, Cu, As and Pb. Cold season samples tended to be more cytotoxic than warm season ones. | (H. Li et al., 2022) |
| A549+HUVEC on chip | PM2.5, 100μg/mL, 24h, SUB | ↑ ROS, IL-1α, IL-1β, IL-6, INF-α, % apoptotic cells, BIP, PERK, p-eIF2α, CHOP, caspase-3 | Co-treatment with 10mM **NAC** reversed oxidative stress, apoptosis and ER stress. | (Guan et al., 2021) |
| A549,  SD-1 | PM2.5, 100μg/mL, 12h, SUB | ↑ ROS, Ca2+, *IL-1β, IL-6, TNF-α, NLRP3, caspase-1, TRPM2* | Pre-treatment with 5mM **NAC** for 1h counteracted the PM2.5-induced increases in ROS, Ca2+ and TRPM2. Confirmed in mice (intratracheal instillation), supporting that ROS activates NLRP3 and its downstream signaling. | (C. Wang et al., 2020) |
| A549, RAW 264.7 | PM, 50μg/mL, 24h, SUB | ↑ ROS, NO, O2-, IL-6, TNF-α, NF-κβ, cells in G2/M, % apoptotic cells  ↓ viability | The authors conclude that PM leads to ROS production that in turn triggered cytokine production and NF-κβ up-regulation but the different experiments were performed using different cell lines and there was no clear link between the events. | (Guerra e Oliveira et al., 2022) |
| A549+ diff THP-1 | Cow stable dust, 25-100μg/mL, 18h, SUB | ↑ ROS, IL-6, TNF-α, cells in G1/G0  ↓ metabolic act, cell in S-G2/M | The decreased metabolic activity and number of cells S/G2 (proliferating) together with increased inflammatory mediators may indicate activation of defense mechanisms. | (Martikainen et al., 2021) |
| A549  BEAS-2B | CSE, 3 (A549) 1.38% (BEAS-2B), 48h, SUB | ↑ p-NF-κβ/NF-κβ, vimentin, N-cadherin, α-SMA  ↓ Cell viability, Nrf2, SIRT1, p-β-catenin/β-catenin, E-cadherin | Post-treatment with **Piperine** 1.25 or 6.25μM for 1h partially restored cell viability and reverted the CSE-induced effects, including EMT activation. | (Saha et al., 2022) |
| BEAS-2B | 3 ≠ functionalized carbon black vs carbon black (PM2.5), 1.56-25μg/mL, 24h, SUB | ↑ *IL-1β, IL-6*, protein carbonylation  ↓ Cell viability, *SOD2, Nrf2* | Functionalized carbon black particles as surrogates for synthetic soot. Highest surface oxygen % and carboxylic acid content seemed to yield stronger oxidative and inflammatory response. Carbon black was the least toxic, only inhibiting *Nrf2*. | (Housseiny et al., 2020) |
| BEAS-2B | CSE, 8%, 24h, SUB | ↑ ROS, MDA, ERK p-p38 MAPK, IL-6, TNF-α, MMP-9, mitochondrial fission factor  ↓ SOD and GPx activity, OPA1 | Pre-treatment w/ 100μM **SS-31** for 1h alleviated CSE-induced oxidative and inflammatory effects. Confirmed in mice (inhalation?). | (Yang et al., 2021) |
| BEAS-2B | CSE, 5%, 24h, SUB | ↑ ROS, apoptotic cells, Bax, cleaved caspase-3/caspase-3, cleaved PARP/ PARP, MDA, TNFα, IL-6, IL-1β  ↓ cell viability, Bcl-2, SOD, GSH-Px, ANXA1, FRP2, pAMPK/AMPK | Pre-treatment with 10μM **methylprednisolone** up-regulated Annexin-A1 expression and suppressed oxidative stress, inflammation and apoptosis via FPR2/AMPK pathway | (Yu & Zhang, 2022) |
| BEAS-2B | CSE, 5%, 24h, SUB | ↑ ROS, MDA, Nrf2, *HO-1, NQO1*, TRIM25, caspase-1, LDH, NLRP3, GSDMD-N, IL-1β, IL-18  ↓ cell viability, SOD-1, SOD-2, SOD-3, Keap-1 | Co-treatment w/ 50μM **(−)-Epicatechin** for 24h alleviated the CSE-induced NLRP3-mediated inflammation and pyroptosis through repressing the oxidative stress via induction of Nrf2. Confirmed in rats (inhalation). | (Tian et al., 2021) |
| BEAS-2B | CSE (1%, 7days) & PM10 (SRM 1648 100μg/mL, 24h) alone vs combined, SUB | ↑ ROS (combined exposure), LDH (not CSE), MDA, IL-6, IL-8, p-ERK, p-JNK, Nrf2, *IL-1β, IL-6, IL-8, TNF-α, MCP-1*, *CXCL-1*, *HO-1, NQO1*  ↓ Cell viability (not CSE), GSH, *TXN* | Exposure to PM aggravated CSE-induced oxidative stress, inflammation, and cell death (but not through apoptosis) in bronchial epithelial cells, suggesting that smokers that live in highly polluted areas may be at higher risk. **Sulforaphane** or **sulforaphane** **N-acetylcysteine** (after exposure to CSE and/or PM10) suppressed the oxidative stress and inflammatory effects of CSE and PM10 by further enhancing Nrf2 signaling. | (Son et al., 2020) |
| BEAS-2B | PM SRM 1649b, 200μg/mL, 24h, SUB | ↑ ROS, IL-6, IL-8, p-IκBα/IκBα, p-p65/p65 NF-κβ, Nrf2, HO-1, NQO1  ↓ Keap1 | Pre-treatment w/ 10ng/mL **FGF10** for 1h resulted in antioxidant and anti-inflammatory effects through ↑Nrf2 signaling and ↓NF-κβ. Similar results were obtained 2.5mM **NAC** or w/ 5μM **BAY11-7082**, an NF-κβ inhibitor. Confirmed in mice (intratracheal instillation). | (Q. Wang, Shi, et al., 2022) |
| BEAS-2B | PM SRM 1649b, 200μg/mL, 24h, SUB | ↑ ROS, Pi+ cells, NLRP3, ASC, GSDM-N/GSDMD, cleaved caspase-1/caspase-1, caspase-1 act., LDH release, mature IL-1β/IL-1β, mature IL-18/IL-18, Nrf2 (total + nuclear), NQO1, HO-1, p-Akt/Akt  ↓ cell viability | Pre-treatment with 10ng/mL **FGF10** for 1h alleviated PM-induced oxidative damage and pyroptosis through activation of PI3K/Akt/Nrf2. Confirmed in mice (intratracheal instillation). | (L. Liu et al., 2022) |
| BEAS-2B | PM2.5 (SRM 2786), 20μg/cm2, 36h, SUB | ↑ Lipid ROS, ROS, MitoMP, Mitochondrial ROS, NADP+/NADPH, COX2, MDA, IL-6, IL-8, TNF-α, Fe2+ accumulation, LC3B-II, NCOA4, FTH1  ↓ cell viability, GPX4, GSH, GPx, Nrf2, PPAR-γ | Pre-treatment with **NaHS** (donor of hydrogen sulfide) alleviated ferroptoptic changes, activated the expression of Nrf2 and PPAR-γ, inhibited ferritinophagy markers. Confirmed in mice (intratracheal instillation). | (Y. Wang, Liao, et al., 2022) |
| BEAS-2B | PM2.5 (China) soluble extract, 300μg/mL (~94 μg/cm2), up to 24h, SUB | ↑ ROS, *IL-1β, IL-6, IL-8, GM-CSF*, cleaved PARP, cleaved caspase-3, Bax, %apoptotic cells, COX2, p-p65 NF-κβ, p-ERK, p-p38 MAPK/ERK, p-JNK  ↓ cell viability, *ZO-1*, *E-cadherin*, Bcl-2, GSH activity, p-mTOR | Soluble PM2.5 extract disrupted the barrier function, induced apoptosis and the release of pro-inflammatory cytokines, as well as activation of the NF-κβ. Confirmed in mice (intranasal instillation). | (Zhao et al., 2020) |
| BEAS-2B | PM2.5, 25-200μg/mL, 24h, SUB | ↑ Nrf2, NF-κβ, *IL-1, IL-6, IL-8, α-SMA*  ↓ Cell viability (lower in direct exp), E-cadherin | BEAS-2B directly exposed to PM2.5 or indirectly exposed to supernatant from PM2.5-treated macrophages (THP-1). While direct exposure had a stronger effect on viability, indirect stimulation w/ high PM2.5 conc strengthened the inflammatory response, and low conc favored EMT phenotype of BEAS-2B. | (Y. Wang, Zuo, et al., 2022) |
| BEAS-2B | PM2.5-0.3 vs organic extractable & non-extractable fractions, 12μgEq. PM/cm2, 6-48h, SUB | ↑ ROS, *Nrf2,* Nrf2 binding activity*, Keap-1, NQO1, HO, SOD,* GSSG/GSH, DNA damage protein carbonylation, 8-isoprostane, TNF-α, IL-6, IL-8, MCP-1, caspase 3/7, caspase 8, caspase 9  ↓ cell viability, ATG5, Beclin, LC3B-II | Both whole PM2.5-0.3 and its fractions induced oxidative stress, inflammation and apoptosis in BEAS-2B cells, but PM2.5-0.3 was in general more toxic than its organic extractable and non-extractable fractions. | (Badran et al., 2020) |
| BEAS-2B, WL-38, Primary rat alveolar macrophages | PM2.5, 70μg/mL, 24h SUB | BEAS-2B:  ↑ ROS, apoptosis rate, collagen I/III, α-SMA, TGF-β1, p-Smad2  ↓ cell viability  WL-38:  ↑ ROS, apoptosis rate, collagen I/III, α-SMA, TGF-β1, p-Smad2  ↓ cell viability  Alveolar macrophages:  ↑ ROS, apoptosis rate, M2 phenotype, mTORC1, TIPE2  ↓ cell viability, M1 phenotype | Co-treatment w/ 5mM **NAC** for 24h could reverse all the effects observed in the alveolar macrophages, suggesting that the PM2.5-induced M2 polarization was caused by oxidative stress. The PM2.5-induced airway remodeling markers in BEAS-2B and WL-38 were also reverted by NAC treatment, indicating that airway remodeling was also dependent on ROS production. Confirmed in rats (inhalation). | (H. Liu et al., 2022) |
| BEAS-2B,  Primary mouse tracheal epithelial cells | PM2.5, 100μg/mL, 24h, SUB | ↑ ROS, MDA, *miR-155*  ↓ SOD, GPx, FOXO3a, *SOD2, CAT* | Pre-treatment w/ 16μg/mL **ECC-BYF** or **NAC** (500μM) for 24h resulted in significant antioxidant activity via down-regulation of miR-155, which lead to FOXO3a up-regulation and decreased ROS. Confirmed in rats (inhalation). | (J. Li et al., 2021) |
| BEAS-2B,  Primary human small airway epithelial cells | Polycarbonate (PC) vs polyurethane (PU) incinerated thermoplastics & derivatives w/ 3% carbon nanotubes (CNT), 0.6 or 1.2μg/cm2, 48h, ND | ↑ ROS (only for PC-CNT and results in DNA damage), LDH, CYP1 act, cells in G2  ↓ viability, cells in G1, mitochondrial membrane potential | When exposing the cells to the particles’ supernatant (filtration, where the PAHs would be) no cytotoxicity was observed. BEAS-2B were more sensitive to the toxic effects of aerosolized incinerated thermoplastics than the small airway cells. 3% CNT exacerbated PC toxicity, especially regarding DNA damage. The PU thermoplastics did not cause toxicity. | (Coyle et al., 2020) |
| BEAS-2B, NHBE cells | Poultry organic dust extract, 0.25%, up to 24h, SUB | ↑ ROS, mitoROS, pro-IL-1β, IL-8, IL-6, PTGS2, ICAM-1, p-p65 NF-κβ, p-STAT-3  ↓ p47phox (indicates NOX2 activation) | The results show that NOX- (particularly NOX2) and XO-derived ROS (not mitochondrial) contribute to the induction of inflammatory mediators. NOX inhibitors VAS2870, GKT137831 and ML171 suppressed ROS production induced by the dust extract. Confirmed in mice (intranasal instillation). | (Meganathan et al., 2022) |
| BEAS-2B, THP-1 | Organic dust extract, 5%, 24h, SUB | BEAS-2B:  ↑ ROS, RNS, *Nrf2,* IL-1β, IL-6, IL-8, IL-10  THP-1:  ↑ ROS, RNS, *iNOS, Nrf2, Trl2, Trl4*, IL-6, IL-8, *NF-κβ* | Pre-treatment w/ **NaHS** (donor of hydrogen sulfide) for 3h alleviated the oxidative stress but not the inflammatory response in vitro. The authors report a clear dissonance between the in vivo (mice, intranasal instillation) and in vitro studies that could relate to interspecies differences and conclude that pre-exposure to H2S modulates lung inflammatory response. | (Shrestha et al., 2021) |
| 16-HBE | CSE, 5%, 24h, SUB | ↑ ROS, LDH, IL-1β, IL-18, Pi+ cells, caspase-1 activity, NLRP3  ↓ GSDMD | **NAC** reversed all the observed effects. The NAC-induced decrease in NLRP3 mRNA expression suggests that NLRP3 activation requires the production of ROS. Confirmed in mice (inhalation). | (Zhang et al., 2021) |
| 16HBE | PM2.5 (China); 67.5, 116.9, 202.5μg/mL; 4 & 24h, SUB | ↑ ROS, LDH, MDA, HO-1, DNA damage  ↓ Cell viability, GSH | PM2.5 also induced DNA damage and influenced DNA repair genes. | (Niu et al., 2020) |
| 16HBE14o-, NuLi-1 | SRM 2585 (Organic extract of house dust), 0.2μg/mL, SUB | ↑ ROS, mitochondrial dysfunction  ↓ TEER | PM affected cell bioenergetics. Oxidative stress is not due to a single fraction but to many of the 22 fractions obtained. Highlights the need to carefully select the cells/cell lines because different results were obtained in terms of cytokine release. | (Marques dos Santos et al., 2022) |
| HBECs | PM SRM 1649b, 300μg/mL, 24h, SUB | ↑ ROS, *IL-6, IL-1α, IL-1β*, COX2, p-p65/p65 NF-κβ  ↓ MitoMP | The inflammatory effects were NF-κβ-mediated. Pre-treatment w/ 500μM **Edaravone** for 1h inactivated NF-κβ, therefore decreasing inflammatory cytokines and ROS generation, while increasing the MitoMP (attenuated mitochondrial dysfunction). Confirmed in mice (intratracheal instillation). | (Zeng et al., 2022) |
| HBECs | PM SRM 1649b, 200μg/mL, 24h, SUB | ↑ ROS, ATF4, GRP78 (Bip), CHOP, ATF6, cleaved caspase-3, NLRP3, ASC, GSDMD-N, IL-1β, caspase-1, IL-18, IL-6, IL-8, apoptotic and necrotic cells, Nrf2 (total and nuclear), HO-1, NQO1. | Pre-treatment with 50μM **Glycyrrhizin** for 1h alleviated all the observed effects. The Nrf2-mediated antioxidative effect of GL regulated ER stress and NLRP3 inflammasome-mediated pyroptosis in PM-exposed cells. Confirmed in mice (intratracheal instillation). | (Shi et al., 2023) |
| HBECs | CSE, 2%, 48h, SUB | ↑ ROS, apoptosis rate, IL-8, IL-6, TNF-α, cleaved caspase-3, p-NF-κβ, Keap-1, Bip/GRP78, p-PERK, p-IRE1α, ATF6, ATF4, CHOP, *NOX1, NOX2, NOX4, XO, Keap-1*  ↓ Cell viability, *HO-1, NQO-1, SOD, GCLM,* Nrf-2 | Co-incubation with **Ephedrine** 10μg/mL alleviated the CSE-induced apoptosis, inflammation and oxidative stress, in a Nrf2-independent manner, by blocking ER-stress. Bip/GRP78 over-expression potentiated all the effects. Confirmed in mice (inhalation). | (H. L. Wang, Chen, et al., 2022) |
| HBSM | CSE, 2.5% 24h, SUB | ↑ proliferation rate, BrdU incorporation (into newly synthesized DNA of actively proliferating cells), cyclin D1, α-SMA, p-SMAD2, p-SMAD3, TGF-β1  ↓ PPAR- γ | 1h pre-treatment w/ Artesunate 100μM up-regulated PPAR-γ, decreased TGF-β1/ Smad2/3 phosphorylation, and suppressed cell proliferation through the TGF-β1/ Smad2/3 signaling pathway by targeting PPAR-γ. Confirmed in rats (inhalation). | (Pan et al., 2021) |
| J774A.1 | CSE, 0.5%, 24h, SUB | ↑ ROS, NO  ↓ Cell viability | Effects reversed by co-treatment with 10μM **quercetin** for 24h. Confirmed in mice (inhalation). | (da Silva Araújo et al., 2020) |
| L-132 | CSE, 10%, 24h, SUB | ↑ TXNIP, NLRP3, mitoROS, LDH release  ↓ cell viability, mitophagy (mitochondria clearance) | Pre-treatment with 40 μM **melatonin** during 1h protected against the CSE-induced cell death, ER-stress mediated inflammasome activation, but only partially decreased ROS production. **NAC** 10mM, when combined w/ melatonin, abolished ROS generation and further decreased the expression of TXNIP and NLRP3. Confirmed in mice (inhalation?). | (Mahalanobish et al., 2020) |
| MH-S | CSE, 3%, 1h, SUB | ↑ ROS, EVs conc, vesicular (not intracellular) SOCS3  ↓ 20S proteasome act. | Pre-treatment with 50μM **NAC** for 1h reversed the effects induced by CSE, supporting that the observed effects are ROS-dependent. Also, proteasome inhibition by bortezomib displayed the same effects as CSE and proved that the increased SOCS3 secretion in EVs derives from 20s proteasome inhibition. | (Haggadone et al., 2020) |
| MLE-12 | PM2.5, 100μg/mL, 24h, SUB | ↑ *α-SMA*, *Txnip,* p-mTOR  ↓ cell viability, *E-cadherin, Txnrd1* | Co-incubation w/ 20μM **Epigallocatechin gallate** for 24h alleviated the oxidative stress (Txnrd1) and EMT induced by PM2.5 via inhibition of AKT/mTOR pathway. Confirmed in mice (intranasal instillation). | (Zhongyin et al., 2022) |
| NCI-H292 | CSE, 10%, 48h, SUB | ↑ IL-8, TNF-α, MMP-9, STAT3, JAK1, JAK2  ↓ SOD, TIMP-1, PPAR | Co-treatment w/ **Tiaobu Feishen formulae** 20% for 48h alleviated the CSE-induced oxidative stress. | (Haoran et al., 2020) |
| NCI-H292,  HPAEC | PM2.5, 10μg/cm2, up to 24h, SUB | ↑ ROS (sub-urban), *HO-1, SOD-2, IL-8* in both cell types but higher in endothelial | Distinct chemical signature was observed between the PM obtained in urban (traffic) and in suburban (biomass burn) areas. Oxidative potential of the PM was also assessed in acellular assays and seemed to be proportional to the PM composition rather than PM concentration, and predictive of cellular oxidative and pro-inflammatory responses | (Crobeddu et al., 2020) |
| NCI-H460 | PM10, 400μg/mL, 12h, SUB | ↑ ROS  ↓ cell viability | Pre-treatment with **quercetin** (conc. ND), **naringin** (800μg/mL) or ***Citrus junos* peel extract** (800μg/mL) for 1h prevented ROS generation and enhanced cell viability. Confirmed in mice (intranasal instillation). | (Lee et al., 2022) |
| NHBE | CS diluted in clean air, 0.5-4L/min, 40’/day \* 3x/week \* 4weeks followed by a 20day-recovery phase (RP), ALI | ↑ HO-1 (back to basal after RP), IL-1β, IL-1 receptor antagonist, IL-6, IL-8, G-CSF, RANTES, CK6, involucrin, TEER, *PPARγ*  ↓ GSH/GSSG (acute exposure), IL-7, MCP-1, MMP-1, MMP-2, MMP-3, MMP-7, MMP-10, MMP-13, MUC5AC, MUC5B, CCSP, cilliated cells, goblet cells, number of cilia, cilia lenght, cilia beating frequency, | Transcriptomics-based study on an in vitro model w/ repeated ALI exposure regimen. Most of the effects were reverted after a 20-day RP, except for IL-6, MMP10, MMP-12, mucin secretion, ciliary abnormalities. Good in vitro emulation of the CS-induced human chronic obstructive pulmonary disease. | (Xiong et al., 2021) |
| Primary human bronchial epithelial cells | DEP alone (12.5 μg/cm2, 3’/day x3days) vs single combined exposure w/ NO2 (0.1ppm) and w/ SO2 (0.2ppm), aerosol | Alone:  ↑ *IL-6, IL-8, TNF-α, GSTA1, HO, SOD3*  ↓ IL-8, MMP-9  Combined:  ↑ *TNF-α, GSTA1, SOD3*, MMP-9 | Repeated exposures to DEP and single combined exposure to DEP and gases induced more significant oxidative stress and inflammation than repeated exposures to gaseous pollutants alone. | (Upadhyay et al., 2022) |
| Primary human CCR6+Th17 cells | CSE, 5%, 48h, SUB | ↑ ROS, SA-β gal+ cells, p16INK4a + cells, *VEGF*α, p-ERK+ cells, *HO-1*, *NQO1* | CS induced ROS-dependent premature senescence of mucosa-homing CCR6+Th17 cells.  Pre-treatment w/ 10mM **NAC** for 1h30 reverted all the effects, supporting their relationship with the CSE-induced ROS generation. | (Baskara et al., 2020) |
| Primary rat alveolar epithelial cells | CSE (Heat-not-burn), 20% *vs*  CSE (conventional), 10%, up to 24h, SUB | ↑ Nrf2, HO-1, GSTA1, GSTA3, NQO1 | No difference between both types of cigarettes. The defense response against oxidative stress was more activated in alveolar type II than type I-like cells. | (Ito et al., 2020) |
| Rat ATII cells, NR8383 | PM2.5, 50μg/mL, 24h, SUB | ↑ ROS, IL-6, TNF-α, apoptosis or necrosis  Data related to immunomodulation is normalized to PM2.5 making it not possible to understand the effects of PM2.5 relative to control. | EVs and **antioxidant-EVs** (containing Nrf2 mRNA and protein) derived from rat adipose-derived stem cells decreased ROS, apoptosis, MDA and favored M2 phenotype, therefore displaying antioxidant and anti-inflammatory properties. Confirmed in rats (intratracheal instillation). | (Gao et al., 2021) |
| RAW 264.7 | PMET720 (common stainless-steel wire) aerosols collected @50 or 60 psi, up to 200μg/mL, 24h, SUB  vs. GMA-SS, MMA-SS welding particles | PMET720(60) @200μg/mL:  ↑ LDH, NF-κβ (>3.12ug/mL)  ↓ Cell viability  PMET720(50&60) @100μg/mL:  ↑ ROS, NF-κβ (>3.12ug/mL) | The PMET720 thermal spray coating particulates were less toxic than the welding particles. While both types of particles induced ROS generation, its association with the increased levels of NF-κβ is not explored. Confirmed in rats (inhalation). | (Kodali et al., 2022) |
| RAW 264.7 | PM2.5, 400μg/mL, 24h, SUB | ↑ ROS, MDA, NLRP3, NF-κβ, Bax, apoptotic rate, caspase-1, caspase-3, GSDMD, IL-1β, %cells in G2  ↓ Bcl-2, SOD act., %cells in G1 | Pre-treatment w/ 10mM **NAC** could partially reverse the oxidative stress, apoptosis and pyroptosis induced by PM2.5. Confirmed in mice (inhalation). | (Ren et al., 2022) |
| RAW264.7 | PM (China) urban aerossol, 30μg/cm2, 24h, SUB | ↑ ROS, *TNF-α, IL-1β, IL-6, MIP-2* | Pre-treatment w/ 2.5-10μM **epigallocatechin gallate** or **gallocatechin gallate** for 1h alleviated the urban-aerosol-induced oxidative stress and inflammation. Confirmed in mice (intratracheal instillation). | (Tanaka et al., 2022) |
| diff U937, HMC3 (microglia) | DPM SRM 2975, 25μg/mL, 24h, SUB  Conditioned serum, 48h, SUB | U937: ↑ ROS, H2O2, MCP-1, IL-1β, IL-6, IL-8, TNF-α  HMC3: ↑ ROS, H2O2, IL-6, IL-8, IL-1β, TNF-α, CD-14 activation | Studying systemic DPM-derived effects to HMC3 by exposing the latter to medium conditioned by U937 previously exposed to DPM. For CD14 activation, this indirect exposure (cytokine diffusion) proved more potent and specific than the direct exposure of HMC3 to DPM. | (Pradhan et al., 2023) |

Act: activity; ADAR: adenosine deaminase acting on RNA; AhR: aryl hydrocarbon receptor; α-SMA: alpha smooth muscle actin; AKT: protein kinase B; ANX: annexin; AMPK: 5' adenosine monophosphate-activated protein kinase; ASC: Apoatfptosis-associated speck-like protein containing a caspase recrutiment domain; ATF: activating transcription factor; ATG: autophagy-related; BAX: Bcl-2-associated protein X; Bcl: B-cell lymphoma; BIP: binding immunoglobulin protein; BrdU: bromodeoxyuridine; CAT: catalase; CCL: CC chemokine ligand; CCR6+: CC chemokine receptor; CCSP: club-cell secretory protein; CD: cluster of differentiation; CHOP: CCAAT/enhancer-binding protein homologous protein; CK: keratin; COX: cycloxigenase; CSE: cigarette smoke extract; CXCL: CXC chemokine ligand; CYBA: Cytochrome b-245 light chain; CYP: cytochrome P450; DEP: diesel exhaust particles; diff: differentiated; DPM: diesel particulate matter; ECC-BYF: effective-component compatibility of Bufei Yishen formula; eIF: eukaryotic initiation factor; EMT: epithelial-mesenchymal transition; EPFR: environmentally persistent free radicals; ER: endoplasmic reticulum; ERK: extracellular signal-regulated kinase; ETS: E26 transformation-specific sequence; EV: extracellular vesicle; FGF: fibroblast growth factor; FOXO: forkhead box protein class O; FRP: N-formyl peptide receptor; FTH: ferritin heavy chain; GCLM: glutamate-cysteine ligase regulatory subunit; GM-CSF: granulocyte-macrophage colony-stimulating factor; GPx: glutathione peroxidase; GPX4: phospholipid hydroperoxide glutathione peroxidase; GRP78: 78 kDa glucose-regulated protein; G-CSF: granulocyte colony-stimulating factor; GMA-SS: gas metal arc- stainless steel; GSDMD: gasdermin D; GSH: reduced glutathione; GSSG: oxidized glutathione; GST: glutathione S-transferase; HO: heme oxygenase; ICAM: intracellular adhesion molecule; IκB: nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor; IL: interleukin; iNOS: inducible nitric oxide synthase; IRE: inositol-requiring enzyme; JAK: Janus kinase; JNK: c-Jun N-terminal kinases; Keap: Kelch-like ECH-associated protein; LC3B: microtubule-associated proteins 1A/1B light chain; LDH: lactate dehydrogenase; MAPK: mitogen-activated protein kinase; MCP: monocyte chemoattractant protein; MDA: malondialdehyde; MEK: mitogen-activated protein kinase kinase; MIP: macrophage inflammatory protein; miR: microRNA; mito: mitochondrial; MitoMP: mitochondrial membrane potential; MMA-SS: manual metal arc stainless steel; MMP: matrix metallopeptidase; mTOR: mammalian target of rapamycin; MUC: mucin; NAC: N-acetylcysteine; NCOA: selective cargo receptor nuclear receptor coactivator; ND: not disclosed; NF-κβ: nuclear factor kappa beta; NLRP: NOD-like receptor family pyrin domain containing; NO: nitric oxide; NOX: NADPH oxidase; NQO1: NAD(P)H dehydrogenase (quinone); Nrf2: nuclear factor erythroid 2-related factor 2; OPA: dynamin-like 120 kDa protein, mitochondrial; p: phosphorylated; p47-phox: Neutrophil cytosol factor 1; PAH: Polycyclic aromatic hydrocarbons; PARP: poly [ADP-ribose] polymerase; PERK: protein kinase R-like endoplasmic reticulum kinase; Pi: propidium iodide; PM: particulate matter; PMET: common consumable stainless-steel wire; PPAR: peroxisome proliferator-activated receptor; PTGS: prostaglandin-endoperoxide synthase; ROS: reactive oxygen species; SA-βgal: senescence-associated β galactosidade; SIRT: sirtuin; Smad: mothers against decapentaplegic homolog; SOCS: suppressor of cytokine signaling; SOD: superoxide dismutase; SRM: standard reference material; STAT: signal transducer and activator of transcription; SUB: submerged; TAC: total antioxidant capacity; TEER: transepithelial electrical resistance; TGF: transforming growth factor; Th17: T-helper lymphocyte; TIMP: tissue inhibitor metalloproteinase; TIPE: TNF alpha induced protein 8 like; TNF: tumor necrosis factor; TRIM: tripartite motif-containing protein; Trl: toll-like receptor; TRPM: transient receptor potential cation channel, subfamily M; TXN: thioredoxin; TXNIP: thioredoxin-interacting protein; TXNRD1: thioredoxin reductase; VEGF: vascular endothelial growth factor; XO: xanthine oxidase; ZO-1: zonula occludens 1.

**References list**

Badran, G., Verdin, A., Grare, C., Abbas, I., Achour, D., Ledoux, F., Roumie, M., Cazier, F., Courcot, D., Lo Guidice, J. M., & Garçon, G. (2020). Toxicological appraisal of the chemical fractions of ambient fine (PM2.5-0.3) and quasi-ultrafine (PM0.3) particles in human bronchial epithelial BEAS-2B cells. *Environmental Pollution*, *263*. https://doi.org/10.1016/j.envpol.2020.114620

Bagam, P., Kaur, G., Singh, D. P., & Batra, S. (2021). In vitro study of the role of FOXO transcription factors in regulating cigarette smoke extract-induced autophagy. *Cell Biology and Toxicology*, *37*(4), 531–553. https://doi.org/10.1007/s10565-020-09556-y

Barzgar, F., Sadeghi-Mohammadi, S., Aftabi, Y., Zarredar, H., Shakerkhatibi, M., Sarbakhsh, P., & Gholampour, A. (2023). Oxidative stress indices induced by industrial and urban PM2.5-bound metals in A549 cells. *Science of the Total Environment*, *877*. https://doi.org/10.1016/j.scitotenv.2023.162726

Baskara, I., Kerbrat, S., Dagouassat, M., Nguyen, H. Q., Guillot-Delost, M., Surenaud, M., Baillou, C., Lemoine, F. M., Morin, D., Boczkowski, J., & Le Gouvello, S. (2020). Cigarette smoking induces human CCR6+Th17 lymphocytes senescence and VEGF-A secretion. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-63613-4

Chen, Y. C., Chuang, T. Y., Liu, C. W., Liu, C. W., Lee, T. L., Lai, T. C., & Chen, Y. L. (2020). Particulate matters increase epithelial-mesenchymal transition and lung fibrosis through the ETS-1/NF-κB-dependent pathway in lung epithelial cells. *Particle and Fibre Toxicology*, *17*(1). https://doi.org/10.1186/s12989-020-00373-z

Coyle, J. P., Derk, R. C., Kornberg, T. G., Singh, D., Jensen, J., Friend, S., Mercer, R., Stueckle, T. A., Demokritou, P., Rojanasakul, Y., & Rojanasakul, L. W. (2020). Carbon nanotube filler enhances incinerated thermoplastics-induced cytotoxicity and metabolic disruption in vitro. *Particle and Fibre Toxicology*, *17*(1). https://doi.org/10.1186/s12989-020-00371-1

Crobeddu, B., Baudrimont, I., Deweirdt, J., Sciare, J., Badel, A., Camproux, A. C., Bui, L. C., & Baeza-Squiban, A. (2020). Lung Antioxidant Depletion: A Predictive Indicator of Cellular Stress Induced by Ambient Fine Particles. *Environmental Science and Technology*, *54*(4), 2360–2369. https://doi.org/10.1021/acs.est.9b05990

da Silva Araújo, N. P., de Matos, N. A., Leticia Antunes Mota, S., Farias de Souza, A. B., Dantas Cangussú, S., Cunha Alvim de Menezes, R., & Silva Bezerra, F. (2020). Quercetin Attenuates Acute Lung Injury Caused by Cigarette Smoke Both In Vitro and In Vivo. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, *17*(2), 205–214. https://doi.org/10.1080/15412555.2020.1749253

Figliuzzi, M., Tironi, M., Longaretti, L., Mancini, A., Teoldi, F., Sangalli, F., & Remuzzi, A. (2020). Copper-dependent biological effects of particulate matter produced by brake systems on lung alveolar cells. *Archives of Toxicology*, *94*(9), 2965–2979. https://doi.org/10.1007/s00204-020-02812-4

Gao, Y., Huang, X., Lin, H., Zhao, M., Liu, W., Li, W., Han, L., Ma, Q., Dong, C., Li, Y., Hu, Y., & Jin, F. (2021). Adipose mesenchymal stem cell-derived antioxidative extracellular vesicles exhibit anti-oxidative stress and immunomodulatory effects under PM2.5 exposure. *Toxicology*, *447*. https://doi.org/10.1016/j.tox.2020.152627

Guan, M., Tang, S., Chang, H., Chen, Y., Chen, F., Mu, Y., Zhao, D., Fan, W., Tian, H., Darland, D. C., & Zhang, Y. (2021). Development of alveolar-capillary-exchange (ACE) chip and its application for assessment of PM2.5-induced toxicity. *Ecotoxicology and Environmental Safety*, *223*. https://doi.org/10.1016/j.ecoenv.2021.112601

Guerra e Oliveira, T., Trancoso, I. A., Lorençoni, M. F., Souza Júnior, A. D., Campagnaro, B. P., Coco, L. Z., Weitzel Dias Carneiro, M. T., do Espírito Santo Lemos, M., Endringer, D. C., & Fronza, M. (2022). Toxicological effects of air settled particles from the Vitoria Metropolitan Area mediated by oxidative stress, pro-inflammatory mediators and NFΚB pathway. *Environmental Research*, *204*. https://doi.org/10.1016/j.envres.2021.112015

Haggadone, M. D., Mancuso, P., & Peters-Golden, M. (2020). Oxidative Inactivation of the Proteasome Augments Alveolar Macrophage Secretion of Vesicular SOCS3. *Cells*, *9*(7). https://doi.org/10.3390/cells9071589

Haoran, D., Xuefang, L., Wanchun, Z., Suxiang, F., Jiansheng, L., Yanqin, Q., Yaosong, W., Yulong, C., Sugai, Y., Peng, Z., & Sux-Iang, F. (2020). Three Tiaobu Feishen formulae reduces cigarette smoke-induced in-flammation in human airway epithelial cells. *J Tradit Chin Med*, *40*(3), 386–392. http://www.journaltcm.com

Housseiny, H. Al, Singh, M., Emile, S., Nicoleau, M., Vander Wal, R. L., & Silveyra, P. (2020). Identification of toxicity parameters associated with combustion produced soot surface chemistry and particle structure by in vitro assays. *Biomedicines*, *8*(9). https://doi.org/10.3390/BIOMEDICINES8090345

Ito, Y., Oshinden, K., Kutsuzawa, N., Kohno, C., Isaki, S., Yokoyama, K., Sato, T., Tanaka, M., & Asano, K. (2020). Heat-Not-Burn cigarette induces oxidative stress response in primary rat alveolar epithelial cells. *PLoS ONE*, *15*(11 November). https://doi.org/10.1371/journal.pone.0242789

Kodali, V., Afshari, A., Meighan, T., McKinney, W., Mazumder, M. H. H., Majumder, N., Cumpston, J. L., Leonard, H. D., Cumpston, J. B., Friend, S., Leonard, S. S., Erdely, A., Zeidler-Erdely, P. C., Hussain, S., Lee, E. G., & Antonini, J. M. (2022). In vivo and in vitro toxicity of a stainless-steel aerosol generated during thermal spray coating. *Archives of Toxicology*, *96*(12), 3201–3217. https://doi.org/10.1007/s00204-022-03362-7

Lee, D. H., Woo, J. K., Heo, W., Huang, W. Y., Kim, Y., Chung, S., Lee, G. H., Park, J. W., Han, B. K., Shin, E. C., Pan, J. H., Kim, J. K., & Kim, Y. J. (2022). Citrus junos Tanaka Peel Extract and Its Bioactive Naringin Reduce Fine Dust-Induced Respiratory Injury Markers in BALB/c Male Mice. *Nutrients*, *14*(5). https://doi.org/10.3390/nu14051101

Li, H., Zhao, Z., Luo, X. S., Fang, G., Zhang, D., Pang, Y., Huang, W., Mehmood, T., & Tang, M. (2022). Insight into urban PM2.5 chemical composition and environmentally persistent free radicals attributed human lung epithelial cytotoxicity. *Ecotoxicology and Environmental Safety*, *234*. https://doi.org/10.1016/j.ecoenv.2022.113356

Li, J., Wang, J., Li, Y., Zhao, P., Tian, Y., Liu, X., He, H., & Jia, R. (2021). Effective-component compatibility of Bufei Yishen formula protects COPD rats against PM2.5-induced oxidative stress via miR-155/FOXO3a pathway. *Ecotoxicology and Environmental Safety*, *228*. https://doi.org/10.1016/j.ecoenv.2021.112918

Liu, H., Nie, H., Lai, W., Shi, Y., Liu, X., Li, K., Tian, L., Xi, Z., & Lin, B. (2022). Different exposure modes of PM2.5 induces bronchial asthma and fibrosis in male rats through macrophage activation and immune imbalance induced by TIPE2 methylation. *Ecotoxicology and Environmental Safety*, *247*. https://doi.org/10.1016/j.ecoenv.2022.114200

Liu, L., Shi, Q., Wang, K., Qian, Y., Zhou, L., Bellusci, S., Chen, C., & Dong, N. (2022). Fibroblast growth factor 10 protects against particulate matter-induced lung injury by inhibiting oxidative stress-mediated pyroptosis via the PI3K/Akt/Nrf2 signaling pathway. *International Immunopharmacology*, *113*. https://doi.org/10.1016/j.intimp.2022.109398

Mahalanobish, S., Dutta, S., Saha, S., & Sil, P. C. (2020). Melatonin induced suppression of ER stress and mitochondrial dysfunction inhibited NLRP3 inflammasome activation in COPD mice. *Food and Chemical Toxicology*, *144*. https://doi.org/10.1016/j.fct.2020.111588

Marques dos Santos, M., Tan Pei Fei, M., Li, C., Jia, S., & Snyder, S. A. (2022). Cell-line and culture model specific responses to organic contaminants in house dust: Cell bioenergetics, oxidative stress, and inflammation endpoints. *Environment International*, *167*. https://doi.org/10.1016/j.envint.2022.107403

Martikainen, M. V., Tossavainen, T., Täubel, M., Wolczkiewicz, K., Lähde, A., & Roponen, M. (2021). Toxicological and microbiological characterization of cow stable dust. *Toxicology in Vitro*, *75*. https://doi.org/10.1016/j.tiv.2021.105202

Meganathan, V., Hamilton, C. E., Natarajan, K., Keshava, S., & Boggaram, V. (2022). NADPH and xanthine oxidases control induction of inflammatory mediator expression by organic dust in the lung. *The FASEB Journal*, *36*(7). https://doi.org/10.1096/fj.202100732R

Niu, B. Y., Li, W. K., Li, J. S., Hong, Q. H., Khodahemmati, S., Gao, J. F., & Zhou, Z. X. (2020). Effects of dna damage and oxidative stress in human bronchial epithelial cells exposed to pm2.5 from beijing, china, in winter. *International Journal of Environmental Research and Public Health*, *17*(13), 1–14. https://doi.org/10.3390/ijerph17134874

Pan, K., Lu, J., & Song, Y. (2021). Artesunate ameliorates cigarette smoke-induced airway remodelling via PPAR-γ/TGF-β1/Smad2/3 signalling pathway. *Respiratory Research*, *22*(1). https://doi.org/10.1186/s12931-021-01687-y

Pang, Y., Huang, W., Luo, X. S., Chen, Q., Zhao, Z., Tang, M., Hong, Y., Chen, J., & Li, H. (2020). In-vitro human lung cell injuries induced by urban PM2.5 during a severe air pollution episode: Variations associated with particle components. *Ecotoxicology and Environmental Safety*, *206*. https://doi.org/10.1016/j.ecoenv.2020.111406

Pradhan, S. H., Gibb, M., Kramer, A. T., & Sayes, C. M. (2023). Peripheral (lung-to-brain) exposure to diesel particulate matter induces oxidative stress and increased markers for systemic inflammation. *Environmental Research*, *231*. https://doi.org/10.1016/j.envres.2023.116267

Ren, F., Xu, J., Zhang, J., Xu, X., Huang, L., Sun, W., Li, R., & Li, F. (2022). PM2.5 induced lung injury through upregulating ROS-dependent NLRP3 Inflammasome-Mediated Pyroptosis. *Immunobiology*, *227*(3). https://doi.org/10.1016/j.imbio.2022.152207

Saha, P., Durugkar, S., Jain, S., Shantanu, P. A., Panda, S. R., Jala, A., Gokhale, S., Sharma, P., & Naidu, V. G. M. (2022). Piperine Attenuates Cigarette Smoke-Induced Oxidative Stress, Lung Inflammation, and Epithelial–Mesenchymal Transition by Modulating the SIRT1/Nrf2 Axis. *International Journal of Molecular Sciences*, *23*(23). https://doi.org/10.3390/ijms232314722

Shi, Q., Qian, Y., Wang, B., Liu, L., Chen, Y., Chen, C., Feng, L., Chen, J., & Dong, N. (2023). Glycyrrhizin protects against particulate matter-induced lung injury via regulation of endoplasmic reticulum stress and NLRP3 inflammasome-mediated pyroptosis through Nrf2/HO-1/NQO1 signaling pathway. *International Immunopharmacology*, *120*. https://doi.org/10.1016/j.intimp.2023.110371

Shrestha, D., Bhat, S. M., Massey, N., Santana Maldonado, C., Rumbeiha, W. K., & Charavaryamath, C. (2021). Pre-exposure to hydrogen sulfide modulates the innate inflammatory response to organic dust. *Cell and Tissue Research*, *384*(1), 129–148. https://doi.org/10.1007/s00441-020-03333-3

So, B., Park, J., Jang, J., Lim, W., Imdad, S., & Kang, C. (2022). Effect of Aerobic Exercise on Oxidative Stress and Inflammatory Response During Particulate Matter Exposure in Mouse Lungs. *Frontiers in Physiology*, *12*. https://doi.org/10.3389/fphys.2021.773539

Son, E. S., Park, J. W., Kim, Y. J., Jeong, S. H., Hong, J. H., Kim, S. H., & Kyung, S. Y. (2020). Effects of antioxidants on oxidative stress and inflammatory responses of human bronchial epithelial cells exposed to particulate matter and cigarette smoke extract. *Toxicology in Vitro*, *67*. https://doi.org/10.1016/j.tiv.2020.104883

Takizawa, M., Nakano, M., Fukami, T., & Nakajima, M. (2020). Decrease in ADAR1 expression by exposure to cigarette smoke enhances susceptibility to oxidative stress. *Toxicology Letters*, *331*, 22–32. https://doi.org/10.1016/j.toxlet.2020.05.019

Tanaka, K. I., Nakaguchi, S., Shiota, S., Nakada, Y., Oyama, K., Sakakibara, O., Shimoda, M., Sugimoto, A., Ichitani, M., Takihara, T., Kinugasa, H., & Kawahara, M. (2022). Preventive Effect of Epigallocatechin Gallate, the Main Component of Green Tea, on Acute Lung Injury Caused by Air Pollutants. *Biomolecules*, *12*(9). https://doi.org/10.3390/biom12091196

Tian, X., Xue, Y., Xie, G., Zhou, Y., Xiao, H., Ding, F., & Zhang, M. (2021). (−)-Epicatechin ameliorates cigarette smoke-induced lung inflammation via inhibiting ROS/NLRP3 inflammasome pathway in rats with COPD. *Toxicology and Applied Pharmacology*, *429*. https://doi.org/10.1016/j.taap.2021.115674

Upadhyay, S., Chakraborty, A., Thimraj, T. A., Baldi, M., Steneholm, A., Ganguly, K., Gerde, P., Ernstgård, L., & Palmberg, L. (2022). Establishment of Repeated In Vitro Exposure System for Evaluating Pulmonary Toxicity of Representative Criteria Air Pollutants Using Advanced Bronchial Mucosa Models. *Toxics*, *10*(6). https://doi.org/10.3390/toxics10060277

Wang, C., Meng, X., Meng, M., Shi, M., Sun, W., Li, X., Zhang, X., Liu, R., Fu, Y., & Song, L. (2020). Oxidative stress activates the TRPM2-Ca2+-NLRP3 axis to promote PM2.5-induced lung injury of mice. *Biomedicine and Pharmacotherapy*, *130*. https://doi.org/10.1016/j.biopha.2020.110481

Wang, H. L., Chen, F. Q., & Wu, L. J. (2022). Ephedrine ameliorates chronic obstructive pulmonary disease (COPD) through restraining endoplasmic reticulum (ER) stress in vitro and in vivo. *International Immunopharmacology*, *103*. https://doi.org/10.1016/j.intimp.2021.107842

Wang, Q., Shi, Q., Liu, L., Qian, Y., & Dong, N. (2022). FGF10 mediates protective anti-oxidative effects in particulate matter-induced lung injury through Nrf2 and NF-κB signaling. *Annals of Translational Medicine*, *10*(22), 1203–1203. https://doi.org/10.21037/atm-22-4389

Wang, Y., Liao, S., Pan, Z., Jiang, S., Fan, J., Yu, S., Xue, L., Yang, J., Ma, S., Liu, T., Zhang, J., & Chen, Y. (2022). Hydrogen sulfide alleviates particulate matter-induced emphysema and airway inflammation by suppressing ferroptosis. *Free Radical Biology and Medicine*, *186*, 1–16. https://doi.org/10.1016/j.freeradbiomed.2022.04.014

Wang, Y., Zuo, X., Jiang, F., Hou, L., Jiang, Q., Zhu, Z., & Tian, L. (2022). A comparative study on the model of PM2.5 direct or indirect interaction with bronchial epithelial cells. *Environmental Science and Pollution Research*, *29*(27), 41567–41576. https://doi.org/10.1007/s11356-021-18324-2

Xiong, R., Wu, Y., Wu, Q., Muskhelishvili, L., Davis, K., Tripathi, P., Chen, Y., Chen, T., Bryant, M., Rosenfeldt, H., Healy, S. M., & Cao, X. (2021). Integration of transcriptome analysis with pathophysiological endpoints to evaluate cigarette smoke toxicity in an in vitro human airway tissue model. *Archives of Toxicology*, *95*(5), 1739–1761. https://doi.org/10.1007/s00204-021-03008-0

Xue, Z., Gao, X., Yu, W., Zhang, Q., Song, W., Li, S., Zheng, X., & Kou, X. (2021). Biochanin A alleviates oxidative damage caused by the urban particulate matter. *Food and Function*, *12*(5), 1958–1972. https://doi.org/10.1039/d0fo02582h

Yang, D. Q., Zuo, Q. N., Wang, T., Xu, D., Lian, L., Gao, L. J., Wan, C., Chen, L., Wen, F. Q., & Shen, Y. C. (2021). Mitochondrial-Targeting Antioxidant SS-31 Suppresses Airway Inflammation and Oxidative Stress Induced by Cigarette Smoke. *Oxidative Medicine and Cellular Longevity*, *2021*. https://doi.org/10.1155/2021/6644238

Yu, C., & Zhang, L. (2022). Methylprednisolone up-regulates annexin A1 (ANXA1) to inhibit the inflammation, apoptosis and oxidative stress of cigarette smoke extract (CSE)-induced bronchial epithelial cells, a chronic obstructive pulmonary disease in vitro model, through the formyl peptide receptor 2 (FPR2) receptors and the adenosine 5’-monophosphate (AMP)-activated protein kinase (AMPK) pathway. *Bioengineered*, *13*(2), 4028–4038. https://doi.org/10.1080/21655979.2022.2031769

Zeng, Y., Zhu, G., Zhu, M., Song, J., Cai, H., Song, Y., Wang, J., & Jin, M. (2022). Edaravone Attenuated Particulate Matter-Induced Lung Inflammation by Inhibiting ROS-NF- κ B Signaling Pathway. *Oxidative Medicine and Cellular Longevity*, *2022*. https://doi.org/10.1155/2022/6908884

Zhang, M. Y., Jiang, Y. X., Yang, Y. C., Liu, J. Y., Huo, C., Ji, X. L., & Qu, Y. Q. (2021). Cigarette smoke extract induces pyroptosis in human bronchial epithelial cells through the ROS/NLRP3/caspase-1 pathway. *Life Sciences*, *269*. https://doi.org/10.1016/j.lfs.2021.119090

Zhao, C., Wang, Y., Su, Z., Pu, W., Niu, M., Song, S., Wei, L., Ding, Y., Xu, L., Tian, M., & Wang, H. (2020). Respiratory exposure to PM2.5 soluble extract disrupts mucosal barrier function and promotes the development of experimental asthma. *Science of the Total Environment*, *730*. https://doi.org/10.1016/j.scitotenv.2020.139145

Zhongyin, Z., Wei, W., Juan, X., & Guohua, F. (2022). Epigallocatechin Gallate Relieved PM2.5-Induced Lung Fibrosis by Inhibiting Oxidative Damage and Epithelial-Mesenchymal Transition through AKT/mTOR Pathway. *Oxidative Medicine and Cellular Longevity*, *2022*. https://doi.org/10.1155/2022/7291774