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Invited Review Article

Redox biology at the intersection of physical activity and air pollution: Mechanisms, consequences, and complexity

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A B S T R A C T

Air pollution and physical inactivity are leading contributors to the global burden of chronic disease and premature mortality. While exercise is a well-established stimulus for physiological adaptations and disease prevention, it also transiently increases reactive oxygen species (ROS) production, which function as essential signals for metabolic remodeling and cellular resilience. In contrast, exposure to air pollution, specifically fine particulate matter ($PM_{2.5}$), leads to sustained and uncontrolled ROS production, promoting oxidative damage, inflammation, and cardiometabolic dysfunction.

This review examines a critical and under-investigated question: How does exercising in polluted environments affect the redox signaling pathways that mediate the health benefits of exercise? We summarize current knowledge at the intersection of exercise physiology, redox biology, and environmental toxicology, with a particular focus on the roles of ROS sources, the scavenger system, and downstream physiological responses. By integrating findings from human and animal studies, we identify factors such as air pollution sources and level of exposure, exercise intensity, and age that shape redox outcomes. We also identify key knowledge gaps to clarify how context-specific redox responses determine whether exercise promotes adaptation or exacerbates pollution-related harm, providing essential insights for future mechanistic research and evidence-based public policies.

1. Introduction

Air pollution and physical inactivity are among the most pressing public health challenges of the 21st century [1]. Air pollution is now recognized as the single most significant environmental risk factor to human health, contributing to over 7 million premature deaths annually [2] through its effects on the cardiovascular and respiratory systems, and on metabolic health [3]. In parallel, insufficient physical activity is a major driver of obesity, type 2 diabetes, cardiovascular disease, and other non-communicable diseases [4]. Both factors disproportionately impact urban populations, and their consequences are projected to increase in the next 25 years [5].

While these two challenges are often addressed separately, their convergence in real-world settings introduces an additional layer of complexity. Physical exercise is one of the most effective interventions for preventing and managing chronic diseases [6]. At the cellular level, exercise stimulates a transient increase in reactive oxygen species (ROS), which serves as a signal to trigger beneficial adaptations [7,8], including enhanced mitochondrial function [9], increased antioxidant defenses [10], and improved metabolic health [11]. Air pollution, particularly the exposure to fine particulate matter <2.5 μm in diameter ($PM_{2.5}$), also elevates cytosolic and mitochondrial ROS, but in a sustained and unregulated manner that promotes oxidative damage and inflammation, leading to aggravated respiratory and cardiometabolic diseases [12]. Furthermore, growing evidence indicates that air pollution accelerates the development of cardiovascular risk factors, such as hypertension, insulin resistance, and obesity [13]. However, it remains unclear whether these effects can be mitigated by physical exercise or are instead exacerbated when exercise is performed in polluted areas.

This overlap in redox-sensitive pathways raises a critical and underexplored question: What happens when exercise is performed in a polluted environment? To what extent can the molecular pathways that mediate exercise-induced adaptations be altered or impaired by pollutant-derived ROS and associated inflammatory signals? This paradox, where exercising under conditions of air pollution may simultaneously promote and undermine health, has significant

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implications for both public policies and physiological research. Epidemiological data suggest that high pollution levels can attenuate [14,15] or even nullify [16] some of the cardiovascular and metabolic benefits of physical activity. Yet, the cellular and redox mechanisms behind these observations remain poorly understood.

In this review, we examine the literature on the molecular link between exercise and exposure to air pollution, with a focus on redox biology. We discuss how transient redox signals mediate exercise-induced adaptations, how air pollution exposure alters redox and inflammatory homeostasis, and how these pathways may interact, synergistically or antagonistically, at the cellular level. Clarifying this interplay is essential for optimizing exercise recommendations in urban and polluted settings, as well as for preserving the full therapeutic and preventive potential of exercise in a changing environment.

2. Transient redox signals in the adaptations to exercise

The term 'ROS' refers to a diverse group of one- and two-electron oxidants, such as superoxide anion ($O_2^{\bullet}$), hydrogen peroxide (H_2O_2), and hydroxyl radical ($^{\bullet}OH$), whose distinct chemical properties, including reactivity, reduction potential, diffusivity, concentration, and subcellular localization, critically influence their biological effects and determine the nature of the cellular response they elicit [17,18]. Among ROS, H_2O_2 is established as a signaling molecule due to its low reactivity and ability to diffuse across membranes [7,18].

The initial observation that free radical levels increase in skeletal muscle during exercise was first reported by Professor Kelvin Davies and colleagues [19] and later confirmed by Professor Malcolm Jackson's group [20], establishing a foundational discovery in the field of redox biology and exercise physiology. While initially considered a harmful byproduct of increased metabolic flux, oxidants were later recognized as essential signaling molecules [21], notably after studies demonstrated that antioxidant supplementation blunts some of the exercise-induced adaptations [11,22,23]. These findings marked a paradigm shift, positioning redox signaling as a mediator of physiological remodeling rather than solely as an agent of oxidative stress [7,24].

Subsequent research has aimed to define the subcellular origin, kinetics, and downstream transduction mechanisms of H_2O_2 during exercise [7]. Although mitochondria have long been considered the primary source of H_2O_2 during muscle contractions, recent studies using genetically encoded, compartment-specific redox biosensors have revealed a more nuanced understanding. Henríquez-Olguín and colleagues demonstrated through redox histology with roGFP-based biosensors that cytosolic NADPH oxidase 2 (NOX2) is essential for the increase in H_2O_2 during a single bout of moderate-intensity exercise [25] and high-intensity interval exercise [26]. These findings were independently confirmed by Kano and colleagues, who used intravital imaging with the HyPer7 biosensor during *in situ* muscle contractions in mice to show NOX2-dependent H_2O_2 production *in vivo* [27]. Mechanistically, NOX2 activation at the sarcolemma induces a rapid and transient increase in cytosolic H_2O_2, which is essential for insulin-independent glucose uptake through the translocation of the glucose transporter GLUT4 [25], as well as for modulating exercise-stimulated gene expression in skeletal muscle [27,28].

Both NOX2 and NOX4 have been implicated in the long-term adaptations to exercise training [29]. Mice lacking NOX2 display impaired mitochondrial remodeling, diminished expression of antioxidant genes, and reduced adaptive responses to repeated bouts of high-intensity interval exercise, including attenuated improvements in running performance [26]. NOX4, which is confined to intracellular membranes including the sarcoplasmic reticulum and mitochondria-associated membranes, is induced by exercise and facilitates ROS-mediated adaptive responses that support muscle function, preserve redox balance, and protect against insulin resistance in the contexts of aging and obesity [29]. These findings collectively establish a framework in which transient exercise-induced H_2O_2, particularly of cytosolic origin, functions as a compartmentalized signal that coordinates both immediate and cumulative metabolic adaptations [7].

A key unresolved question has been how these redox signals are sensed and transduced into durable biochemical changes [30], with post-translational modifications of cysteine thiols by H_2O_2 emerging as essential regulatory mechanisms in cell biology [31,32]. In this context, the cytosolic peroxiredoxin 2 (PRDX2) may function as a redox-sensitive relay that rapidly responds to H_2O_2 and conveys oxidative signals to downstream cysteine-containing target proteins involved in gene expression, mitochondrial adaptation, and cellular stress responses [33–35]. Notably, Professor Jackson's group demonstrated that PRDX2 undergoes rapid and reversible oxidation in response to muscle contractions, suggesting its role as a redox relay that conveys oxidative signals to downstream cysteine-containing target proteins [35,36]. Supporting its functional relevance, PRDX2 is essential for exercise-induced adaptations in *C. elegans*, including mitochondrial remodeling and improved lifespan following exercise training [37,38]. However, whether similar mechanisms operate in mammalian organisms and humans remains to be elucidated. In sum, transient H_2O_2 generation during exercise, primarily driven by NOX2 and NOX4, and its transduction through redox-sensitive cysteine residues, constitutes a pivotal redox signaling axis for skeletal muscle adaptation. This process is defined by spatial specificity, temporal precision, and reversible redox regulation, distinguishing it from the chronic, unregulated oxidative stress induced by overtraining and environmental factors that promote inflammation and metabolic dysfunction.

3. ROS as physiopathological signals in air pollution exposure

Air pollution particulate matter (PM) consists of a complex mixture of liquid and solid particles released directly into the atmosphere that differ markedly in size, chemical composition, and biological impact [39]. PM primarily arises from fossil fuel combustion for power generation, transportation, and industrial processes, and is typically categorized by aerodynamic diameter into coarse particles <10 μm (PM_{10}), fine particles <2.5 μm ($PM_{2.5}$), and ultrafine particles <0.1 μm (UFP). Each PM fraction exhibits distinct deposition profiles within the respiratory tract and varying capacities to reach systemic circulation. $PM_{2.5}$ is primarily categorized (and regulated) based on aerodynamic diameter, reaching a global average urban $PM_{2.5}$ concentration of ~35 μg/m^3 [40,41]. Notably, $PM_{2.5}$ toxicological potential is more closely linked to its chemical composition. In particular, the presence of redox-active organic compounds (e.g., Polycyclic Aromatic Hydrocarbons, PAHs; Polychlorinated biphenyls, PCBs) and transition metals (e.g., Fe, Ni, Cr, V) significantly enhances its oxidative potential, which contributes more directly to its harmful biological effects than size alone [42]. By acting as a carrier for these toxic constituents deep into the respiratory tree, inhaled $PM_{2.5}$ initiates local oxidative stress and inflammatory responses, establishing a vicious cycle that Valacchi and colleagues termed 'oxinflammation' [43,44]. This redox-driven upregulation of innate immune pathways contributes to the onset and progression of respiratory diseases, including chronic obstructive pulmonary disease (COPD), respiratory infections, and lung cancer, all of which exhibit a positive association with ambient $PM_{2.5}$ levels in human populations [45,46]. The effects of $PM_{2.5}$ can also extend systemically to distal organs [47], with proposed transmission mechanisms including the release of inflammatory mediators and oxidized lipids into the bloodstream, together with autonomic nervous system imbalance, which collectively promote vascular dysfunction and disrupt tissue homeostasis in the periphery [48]. In parallel, UFP can cross the blood–brain barrier, ultimately accessing the brain and contributing to neuroinflammatory responses in polluted environments [49].

Particle oxidative potential refers to the capacity of PM to induce oxidative stress in biological systems through enhanced ROS production or reactivity with macromolecules. It is most frequently assessed using *in vitro* acellular assays, which quantify the ability of PM samples to oxidize

reductants (e.g., dithiothreitol, DTT) or deplete antioxidants (e.g., glutathione, GSH) [50]. For a more biologically relevant approach, cellular assays evaluating the activation of nuclear factor E2-related factor 2 (Nrf2) and the nuclear factor kappa B (NF-κB), typically in cell types that are the first to encounter inhaled PM (i.e., alveolar epithelial cells and macrophages), are recommended [51]. The chemical composition of PM, and thus its oxidative potential, is largely dictated by emission sources, such as stationary (power plants, refineries, factories) or mobile (traffic-related, construction). Compared with biogenic and crustal sources, anthropogenic emissions yield PM with higher oxidative potential [42] and greater health risk [52]. Given the heterogeneous nature of PM, experimental research uses collected Concentrated Air Particles (CAPs), Diesel Exhaust Particles (DEP), Residual Oil Fly Ash (ROFA), and commercially available Standard Reference Materials (SRM) provided by the US National Institute of Standards and Technology (NIST) [39]. Notably, while particle oxidative potential has been associated with acute health effects, the specific PM characteristics driving chronic health outcomes remain less well defined.

Gaseous co-pollutants, including nitrogen oxides (NOx), sulfur dioxide (SO_2), carbon monoxide (CO), and ozone (O_3), further contribute to adverse health effects and can act synergistically with $PM_{2.5}$ during air pollution exposure [53]. In urban environments, ground-level O_3 is formed through complex photochemical reactions between NOx and volatile organic compounds (VOCs) in the presence of sunlight, and has been linked to both short- and long-term adverse health outcomes [54,55]. Nitrogen dioxide (NO_2) serves as an indicator of traffic-related air pollution and has been associated with a wide spectrum of diseases, including musculoskeletal disorder [56]. Whether NO_2 itself drives these associations or reflects the influence of co-pollutants remains uncertain. While beyond the scope of this review, the combined impact of other environmental stressors, such as noise and light pollution [57], worsen the health burden in urban areas [58] and might also influence the physiological responses to physical activity.

While the respiratory tract is the first point of contact for airborne pollutants, most morbidity and mortality linked to $PM_{2.5}$ exposure arises from cardiovascular diseases (CVD) [59], particularly ischemic heart disease (IHD) and stroke, and occurs even at concentrations below current air quality standards [60]. O_3 seems to act synergistically with $PM_{2.5}$ in their association with CVD mortality, particularly in cities located at higher latitudes and with lower annual mean temperatures [61]. Over the past decade, it has become increasingly evident that $PM_{2.5}$ may also contribute to CVD pathogenesis at earlier stages, including during the development of major risk factors such as hypertension, insulin resistance, and obesity [62]. The interplay between redox and inflammatory pathways triggered by $PM_{2.5}$ exposure, and their relevance to both CVD and its risk factors, is now well established [63,64]. However, although regular physical exercise is fundamental to cardiovascular health and the management of CVD risk factors, exercising in a polluted environment may attenuate these benefits or even prove detrimental [16]. In fact, the bidirectional relationship between air pollution and physical exercise remains poorly understood. Given that physical exercise often occurs outdoors, understanding the interaction between $PM_{2.5}$ exposure and the physiological response to exercise is critical.

Current evidence has identified well-characterized mechanisms underlying the biological responses triggered by $PM_{2.5}$ exposure, primarily involving oxidative stress and inflammation. In the lung, alveolar macrophages readily uptake $PM_{2.5}$, leading to sustained NOX2 activation and impaired mitochondrial function [65,66]. At early stages, $PM_{2.5}$ exposure triggers antioxidant responses mediated by Nrf2, leading to the upregulation of superoxide dismutase (SOD) and heme oxygenase-1 (HO-1) [67]. With sustained exposure, redox disturbances activate NF-κB signaling [68], which drives production of inflammatory cytokines, such as TNF-α, IL-6, and CCL2, along with NLRP3 inflammasome activation and subsequent release of IL-1β and IL-18 [69]. Indirectly, $PM_{2.5}$ induces macrophage inflammation through TLR4 signaling, which is triggered by oxidized macromolecules acting as danger-associated molecular patterns (DAMPs), such as oxPAPC [70]. Interestingly, oxPAPC also promotes hypothalamic inflammation and insulin resistance, linking neuroinflammatory responses with altered metabolic health following $PM_{2.5}$ exposure [71]. Together, these findings illustrate the complex dose-response relationship between $PM_{2.5}$ and redox homeostasis, where pro-oxidant and antioxidant responses interact dynamically [72]. Once antioxidant defenses are overwhelmed, the balance shifts toward enhanced leukocyte recruitment in the lungs and systemic propagation of inflammatory responses [73].

While most mechanistic insights are derived from murine models, evidence for similar inflammatory and oxidative stress profiles has been reported in humans. For example, circulating levels of inflammatory mediators that positively correlate with $PM_{2.5}$ exposure include IL-1β, TNF-α, IL-6, and CCL2, which promote monocytosis and the upregulation of adhesion factors, such as intracellular cell adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) [74]. In a natural experiment, human exposure to $PM_{2.5}$ has also been associated with increased circulating biomarkers of lipid peroxidation [75]. These findings, among others, validate the upregulation of local and systemic inflammatory and oxidative stress pathways in humans following exposure to $PM_{2.5}$.

Complementing these observations, studies in rodent models have demonstrated that $PM_{2.5}$-driven pulmonary inflammation and oxidant production favor leukocyte trafficking and vascular inflammation in the periphery [76,77]. In addition, $PM_{2.5}$-induced endothelial dysfunction is aggravated by reduced nitric oxide (NO) bioavailability, attributed to NOX2 activation [52] and eNOS uncoupling [78]. Notably, impaired vascular redox homeostasis and inflammation have been linked to altered vasomotor tone [79] and insulin resistance [72,80] in $PM_{2.5}$-exposed mice, further supporting the systemic dissemination of $PM_{2.5}$ pathophysiological effects. These may be particularly relevant during exercise, when vasodilation and perfusion responses are crucial for optimal oxygen delivery and muscle function.

Once the response to $PM_{2.5}$ exposure reaches distal organs, it has been associated with inflammation, activation of NOX2 and NOX4, and alterations in mitochondrial ultrastructure and function leading to increased $O_2^{\bullet-}$ and H_2O_2 production, together with reduced ATP levels [81]. For example, in the heart, these changes have been linked to impaired cardiac contractility [81,82], fibrosis [83], enhanced ischemia/reperfusion injury [73], adverse myocardial remodeling [84], and aggravated heart failure [85]. Therefore, exposure to $PM_{2.5}$ compromises myocardial functional reserve, limiting its ability to properly adapt to increased cardiac output. Whether this is also the case for skeletal muscle under conditions of elevated energy demands, such as during physical exercise, is less well understood. Furthermore, exposure to $PM_{2.5}$ promotes macrophage infiltration and increased adiposity in white adipose tissue [79,86,87]. In brown adipose tissue, reduced glucose uptake and uncoupling protein-1 (UCP-1) expression have been associated with decreased energy expenditure in $PM_{2.5}$-exposed mice [86,88]. Given the central role of adipose tissue in energy metabolism and thermoregulation, these alterations could also impair exercise performance or adaptation.

In summary, exposure to $PM_{2.5}$ induces redox, inflammatory, and metabolic changes that are not only confined to the lung but are also evident in key metabolic organs. In the following section, we will explore how these pathways interact with physical exercise in both directions.

4. Interplay between air pollution and physical activity in human cohort studies

Globally, an estimated 70 % of the population engages in regular physical activity, emphasizing the importance of understanding its physiological consequences under varying environmental conditions

[89]. During moderate-to high-intensity physical activity, ventilation increases proportionally with intensity, reaching values up to ~15-fold greater than at rest [90]. This elevated airflow, coupled with increased pulmonary perfusion, may enhance the susceptibility of the respiratory tract to inhaled pollutants.

While regular physical activity is widely recognized for its protective effects on health, including improvements in cardiorespiratory fitness, vascular function, and metabolic regulation [91], these benefits may be compromised when exercise is performed in polluted environments [92]. Recent large-scale cohort studies have investigated whether regular physical activity can mitigate the adverse health effects of long-term exposure to ambient air pollution, particularly fine particulate matter. Sun and colleagues [16] analyzed data from over 322,000 adults in China to examine how physical activity, through active commuting and farming, interacts with long-term $PM_{2.5}$ exposure. They found that physical activity reduced the risk of cardiovascular disease only in areas with relatively low air pollution ($PM_{2.5} < 54$ μg/m^3). In high-pollution areas ($PM_{2.5} \geq 54$ μg/m^3), these benefits were lost, and in some cases, the health risk increased, particularly for stroke among farmers. This study suggests that high $PM_{2.5}$ exposure can offset or reverse the protective effects of physical activity.

In contrast, evidence from Swedish cohorts suggests that habitual exercise offers some degree of cardiovascular protection, even in polluted environments. In a study of 34,748 adults followed for 12.4 years, higher residential $PM_{2.5}$ and PM_{10} levels were associated with an increased risk of first-time IHD, particularly among individuals who exercised less than twice per week. In contrast, regular exercise was linked to a significantly lower risk of IHD among those exposed to higher PM concentrations, suggesting a protective effect of physical activity in polluted environments [93]. Subsequently, a complementary analysis of 2221 individuals with prior IHD or stroke showed that elevated $PM_{2.5}$ exposure was associated with increased risk of disease recurrence, but only among those with low physical activity levels. Notably, higher exercise frequency was paradoxically linked to increased IHD recurrence in low-pollution settings, though interaction effects were not statistically significant [94]. Together, these studies suggest that regular physical activity may mitigate the cardiovascular effects of air pollution, especially in high-exposure settings, but further research is needed to clarify the risks of exercise in low-pollution contexts and among individuals with prior cardiovascular events.

Similar patterns have emerged for metabolic diseases in Asian cohorts. In Hong Kong, Sun and colleagues [95] reported that higher volumes of physical activity, particularly aerobic and traditional Chinese exercises, were associated with reduced cardiovascular and respiratory mortality regardless of air quality, suggesting that the benefits of physical activity outweighed the risks from chronic $PM_{2.5}$ exposure. In Korea, Kim and colleagues [96] observed that moderate to vigorous physical activity reduced diabetes incidence across both low/moderate and high PM exposure groups, although benefits were slightly attenuated in more polluted areas. In Taiwan, Guo and colleagues [97] showed that high physical activity and low $PM_{2.5}$ exposure jointly conferred the lowest risk of developing type 2 diabetes, but physical activity remained protective even at higher pollution levels.

Collectively, these studies suggest that although air pollution may attenuate some of the health benefits of exercise, regular physical activity remains broadly protective against cardiovascular and metabolic diseases, even in polluted environments. However, as these findings are based on observational data, controlled experimental studies are needed to establish causality and clarify the biological mechanisms underlying these interactions.

4.1. *Acute physiological responses to exercise in polluted environments in humans*

One of the primary physiological responses to physical activity is an increase in minute ventilation (VE), which rises proportionally with exercise intensity [98]. Under polluted conditions, this elevated ventilatory demand promotes greater inhalation and deeper pulmonary deposition of airborne particles. *In silico* lung deposition models for emissions from diesel and compressed natural gas (CNG) buses have shown that total particle deposition increases approximately 5-fold from rest to light exercise (VE: 25 L/min) and about 20-fold during heavy exercise (VE: 50 L/min) [99]. These model-based predictions were supported by findings from Daigle and colleagues, who reported a 4.5-fold increase in UFP deposition at 10–25 μg/m^3 during 2 h of moderate cycling (target VE: 25 L/min/m^2 body surface area) compared to rest in healthy individuals. In a real-world urban cycling study conducted in Vancouver, Canada, particle uptake was 45 % higher on high-traffic routes (7.3 μg/m^3 $PM_{2.5}$ and 13.0 μg/m^3 PM_{10}) compared to residential low-traffic routes (4.4 μg/m^3 $PM_{2.5}$ and 8.8 μg/m^3 PM_{10}) [100]. Collectively, evidence from simulation models, controlled human exposure studies, and real-world observations demonstrates that the elevated ventilatory demands of physical activity substantially increase the pulmonary deposition of PM.

While exercise increases overall PM deposition, exercise intensity may influence the regional distribution of particles within the respiratory tract. Simulation studies indicate that higher intensities promote deposition in the upper airways, moderate intensities in the central airways, and sedentary conditions in the lower airways [101]. In contrast, Bennett and colleagues [102] reported that exercise can enhance bronchial clearance of PM, as shown by reduced retention of a radioactively tagged (^{99m}Tc) monodisperse aerosol with a median aerodynamic diameter of 2.6 μm at 2.5 h after exposure during exercise compared with rest. Overall, physical activity intensity, particle deposition patterns, and physicochemical characteristics of inhaled particles [103] are key determinants of both particle deposition and health outcomes during exercise in polluted environments. Among these factors, UFP and $PM_{2.5}$ pose the highest risk due to their deeper penetration and greater potential to elicit oxidative stress and inflammatory responses. During moderate to vigorous exercise, oral breathing becomes more prominent, bypassing nasal filtration and altering particle deposition patterns across the airways. This shift may influence site-specific redox and inflammatory responses, allowing greater penetration of fine and ultrafine particles into the lower respiratory tract. These considerations also carry practical implications for field studies, where mask design and fit may determine their effectiveness under high-ventilation conditions.

The physiological consequences of PM accumulation during exercise have been examined in a limited number of human studies. In healthy adults, a dose-dependent decline in lung function was observed after exercise in high-pollution conditions but not under low-PM exposure (250,000 vs. 7400 p.m. < 1 μm particles/cm^3) [104]. This decline was accompanied by reduced nitrate (NO_3^-) and exhaled NO levels, together with elevated malondialdehyde (MDA) in exhaled breath condensate, suggesting oxidative injury through a peroxynitrite-mediated lipid peroxidation mechanism [104]. Extending beyond lung function, a controlled-exposure study [105] in 10 healthy adults reported increased neutrophils in bronchoalveolar lavage (BAL) samples after 1 h of intermittent light exercise (VE: 50 L/min) while breathing CAPs (23.1–311.1 μg/m^3) collected from Cape Hill, North Carolina, US. Consistent with this inflammatory response, 13 non-smoking adults exposed for 2 h to alternating bouts of 15 min of light exercise in the Söderleden road tunnel in downtown Stockholm (64 μg $PM_{2.5}$/m^3 and 176 μg PM_{10}/m^3; 230 μg NO_2/m^3) showed elevated alveolar macrophages and lymphocytes in BAL [106].

Real-world evidence supports these experimental data: a field trial with 16 moderately trained cyclists in Antwerp (Belgium), found a modest but significant increase in circulating neutrophils after 20 min of exercise (74 % HRmax) near a highway (24.2 μg $PM_{2.5}$/m^3 and 62.8 μg PM_{10}/m^3) versus clean indoor air (2.0 μg $PM_{2.5}$/m^3 and 7.6 μg PM_{10}/m^3) [107]. Moving from pulmonary to systemic outcomes, another outdoor/indoor comparison under an air quality health index (AQHI) ≥5 (considered a moderate risk) in London, Ontario (Canada), reported

that interquartile increases in $PM_{2.5}$ (mean: 15.2 μg $PM_{2.5}/m^3$) were associated with a 5.6 % increase in urinary MDA and impaired cardiovascular function [108]. Together, these studies show that acute exercise in polluted environments exacerbates both airway and systemic inflammation, with oxidative stress emerging as a central mechanism.

Not all studies report adverse effects under comparable conditions. For instance, in a controlled study, 14 healthy and 12 asthmatic adults exercising at moderate intensity (VE: 20 L/min) were exposed to carbon UFP levels of 10–50 μg/m^3 via a mouthpiece and nose clip system, with no significant changes detected in ventilatory or inflammatory parameters [109]. Likewise, studies with healthy cyclists found no differences in the oxidative stress marker 8-OHdG or in sputum IL-6 and CRP [100], or in circulating IL-6 and IL-8 levels [110], when comparing a low and high traffic-related air pollution exposure in Barcelona, Spain (30.0 μg $PM_{2.5}/m^3$ and 67.8 μg PM_{10}/m^3 vs. 80.8 μg $PM_{2.5}/m^3$ and 129.7 μg PM_{10}/m^3).

When specifically considering the effects of gaseous pollutants, in the MOSES trial, healthy older adults (55–70 years) performed intermittent moderate 15-min exercise while exposed for 3 h to O_3 [111]. Despite increased ventilation during exercise, no significant effects were observed on primary biomarkers of systemic inflammation (CRP, IL-6) or oxidative stress (8-isoprostane). However, endothelin-1, a potent vasoconstrictor, was significantly elevated after exposure to 120 ppb O_3, whereas nitrotyrosine, a marker of nitrosative stress, showed a marginal decrease. Overall, an acute O_3 exposure during exercise did not elicit systemic inflammatory responses in healthy older subjects, but alterations in endothelial function and redox balance suggest potential subclinical vascular effects.

In summary, the current evidence suggests that the interaction between exercise and air pollution is influenced by multiple factors, including individual susceptibility, pollutant dose, and the physicochemical properties of PM. These variables may critically modulate redox signaling pathways and inflammatory responses.

4.2. *Mechanistic studies using experimental animal models of physical exercise and air pollutants*

Experimental preclinical models offer a controlled approach to examine how exercise modulates oxidative stress, inflammation, and cardiovascular function in response to air pollutants. These models help identify underlying biological mechanisms and assess how exercise may either mitigate or exacerbate pollution-related health effects (Fig. 1). This section summarizes key findings, highlighting both protective and adverse outcomes of exercise under polluted conditions.

Experimental mouse models have been particularly useful in testing whether exercise modifies air pollutant-induced oxidative stress and inflammation. For instance, Ávila and colleagues, male Swiss mice underwent daily high-intensity swimming for 30 min over 10 days. During the final 5 days of training and for additional 5 days afterwards, mice received intranasal DEP (30 μg/mouse) derived from São Paulo public transport containing 500 ppm sulfur, PAHs, and transition metals. Exercise attenuated DEP-induced lung GSH depletion and normalized

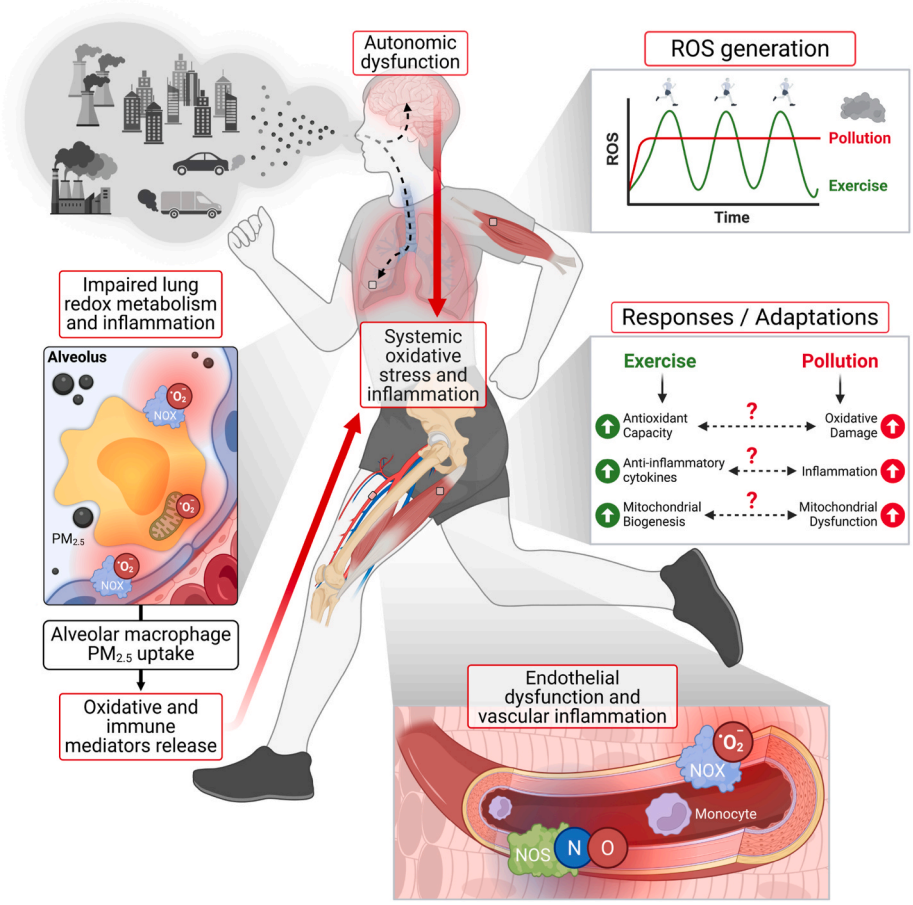

Fig. 1. Interaction between air pollution and physical exercise. Moderate-to high-intensity endurance exercise increases pulmonary ventilation and perfusion, which in polluted environments enhances the deposition and uptake of air pollutants in the lungs. This can lead to enhanced local ROS production and activation of alveolar macrophages that promote a systemic pro-inflammatory response. In parallel, endurance exercise also acutely elevates the production of ROS in skeletal muscle and other tissues, serving as essential signals for adaptive processes such as improved antioxidant defense, mitochondrial biogenesis, and metabolic remodeling.

levels of pro-inflammatory cytokines (IL-1β, TNF-α, IL-6, IFN-γ) compared to sedentary DEP-exposed controls [112].

In a subsequent study, Fan and colleagues trained 7-week-old C57BL/6 mice on a treadmill (12 m/min, 25 % incline) for 24 weeks. The mice were housed in an ambient air exposure chamber in Shanghai, where $PM_{2.5}$ is enriched in PAHs and transition metals [113]. After each training session, mice were exposed for 8 h to either filtered air (mean $PM_{2.5}$: 11.8 ± 4.4 μg/m^3) or ambient $PM_{2.5}$ (mean $PM_{2.5}$: 71.2 ± 45.0 μg/m^3). In the exercise plus $PM_{2.5}$ group, NOX4 mRNA expression was reduced in skeletal muscle and epididymal white adipose tissue after 4 months compared to sedentary $PM_{2.5}$-exposed mice. This reduction remained significant in adipose tissue at 6 months. Concurrently, Nrf2 mRNA expression increased in the exercise group, suggesting an adaptive antioxidant response. These changes were associated with reduced ROS production and preserved redox homeostasis.

Exercise training may help mitigate vascular dysfunction induced by $PM_{2.5}$ exposure. Feng and colleagues investigated this using 6-week-old male Wistar rats subjected to a 6-week treadmill protocol, alternating between low (17 m/min) and moderate (21 m/min) intensity running for 50 min per day, 5 days per week. At week 7, the rats were exposed to $PM_{2.5}$ collected in Beijing, China, via repeated intratracheal instillation at a dose of 3 mg/kg body weight. Compared to sedentary $PM_{2.5}$-exposed controls, the exercised rats exhibited reduced plasma HDL oxidation and elevated NO levels in the thoracic aorta [114]. These findings suggest that regular aerobic exercise enhances antioxidant defenses and promotes vascular adaptations that may counteract $PM_{2.5}$-induced oxidative stress and endothelial dysfunction.

Conversely, Mai and colleagues examined how exercise intensity influences oxidative stress and inflammation under air pollution exposure using 30-day-old B6.129SF2/J mice [115]. Two distinct exercise protocols were applied: moderate-intensity training (60 min of swimming, 5 days per week, with workload gradually increasing to 4 % by week 5) and high-intensity training (initially 20 min per session, 5 days per week, with workload increasing to 8 % by week 9 and duration extended to 60 min). Mice exposed to $PM_{2.5}$ received daily intranasal instillations of 5 μg $PM_{2.5}$ collected from São Paulo, primarily from mobile sources. After 12 weeks, high-intensity training elevated MDA levels in cardiac tissue, irrespective of $PM_{2.5}$ exposure, suggesting increased lipid peroxidation. Despite this, high-intensity exercise induced an anti-inflammatory profile, as indicated by a reduced extracellular-to-intracellular 70 kDa heat shock protein (eHSP70/iHSP70) ratio in plasma. In contrast, moderate-intensity training did not significantly alter the eHSP70/iHSP70 ratio and was associated only with elevated cardiac MDA.

Age appears to be a relevant factor in modulating redox responses to combined exercise and air pollution exposure. Cho and colleagues compared young (1-month-old) and old (12-month-old) male C57BL/6 mice exposed to a transition-metal-rich PM surrogate. Mice received tail vein injections (500 μg PM/kg body weight) three times per week and underwent endurance training consisting of 30 min of exercise, 5 days per week for 8 weeks [116]. In young mice, exercise under PM exposure increased serum CAT and SOD activity and reduced MDA levels compared to sedentary PM-exposed controls, indicating a protective antioxidant response in this group. In contrast, older mice did not show this benefit; instead, there was a trend towards a lower antioxidant capacity relative to their younger counterparts.

Together, these findings support a protective role for exercise training against PM-induced oxidative stress and inflammation. However, the underlying redox mechanisms remain insufficiently defined, as specific ROS species were not directly quantified and the main sources were not identified.

Animal studies modeling physical activity in the context of gaseous pollutant exposure are scarce, particularly for NOx and SO_2. Early work reported that exercising while breathing high levels of NO_2 and O_3 decreases the resistance to respiratory infections in female CD-1 mice [117]. In male Sprague-Dawley rats, enhanced bronchoalveolar permeability was observed when exercising during exposure to NO_2 and O_3 compared with rest, which may partially explain this effect [118]. Unfortunately, redox and inflammatory mechanisms were not further explored in these studies. More recently, Long and colleagues trained male Syrian Golden hamsters on a treadmill for 5 weeks, followed by O_3 exposure at 1.0 ppm for 1 h while running on a customized treadmill. While no changes were observed in the number of neutrophils in the BAL, running during O_3 exposure increased BAL F_2-isoprostane levels without significantly depleting antioxidant defenses [119]. This suggests that physical activity may aggravate O_3-induced lung oxidative stress, with BAL F_2-isoprostanes acting as a useful biomarker for monitoring this interaction. Down this line, Zhao and colleagues trained male Wistar rats on a treadmill at 20 m/min for 1 h per day, 5 days per week, for a total of 8 weeks, while being exposed to 0.14 ppm O_3 twice a week [120]. This moderate-intensity exercise induced a physiological myocardial hypertrophy, but the intermittent O_3 exposure led to pathological changes and increased inflammation in the heart of exercised rats breathing O_3. Conversely, Gordon and colleagues trained female Long-Evans rats on a treadmill for 10 weeks, followed by O_3 exposure at 1.0 ppm for 5 h on 2 consecutive days [121]. Lung inflammation and ventilatory function, together with baseline glycemia, were similarly affected by O_3 in both sedentary and trained rats. However, glucose handling during a glucose tolerance test (GTT) was significantly improved in the trained group exposed to O_3. Taken together, these observations underscore a complex interplay between physical activity and O_3 exposure, in which exercise training may have a protective cardiometabolic effect, but exercising during peak O_3 levels (i.e., during daylight hours in the afternoon) might be detrimental for the cardiorespiratory system.

Although preclinical models enable controlled investigation of the biological effects of air pollution and exercise, their relevance to real-world conditions remains limited. The existing literature reports heterogeneous findings, largely due to inconsistencies in exposure methods, pollutant composition and physicochemical properties, exercise protocols, sampling time points, and experimental settings. This variability limits comparability across studies and underscores the need for systematic approaches that better reflect human patterns of exposure during physical activity. Furthermore, current methods for PM delivery often fail to replicate the dynamics of inhalation, potentially altering particle behavior and toxicity. To inform effective human interventions, future studies should incorporate more physiologically relevant exposure systems and focus on precise characterization of the molecular and cellular pathways involved.

5. Future directions

Advancing our understanding of how air pollution modulates inflammatory and redox responses during exercise requires more rigorously controlled and mechanistically informed studies in both experimental models and human populations. The current evidence base is limited by variability in exposure assessment, exercise protocols, and outcome measures. Building on the studies reviewed in this paper, we outline the following priority areas to guide future research.

- **Standardized and individualized exposure assessment in humans:** Future studies should be adequately powered and carefully designed to monitor and control pollutant load and exposure. Inhaled and deposited doses should be quantified using particle–size–specific deposition models and normalized to individual factors such as body size, ventilation rate, and different exercise modalities. To enable a more personalized approach, incorporating at-risk populations and exposome analysis would provide a comprehensive assessment of the environmental factors that may hinder the health benefits of exercise.
- **Mechanistic dissection in experimental models:** Preclinical studies should prioritize inhalation-based exposure systems over

instillation and consistently report a full physicochemical characterization of air pollutants, including PM oxidative potential. To capture mechanistic insights, experiments should comprehensively assess redox changes, antioxidant defenses, oxidative damage, and redox signaling pathways within the same tissues. Technologies such as genetically encoded redox biosensors, peroxiredoxin dimerization assays, and cysteine redox proteomics should be used to resolve spatial and temporal aspects of redox stress. Source-specific manipulations using pharmacological inhibitors or genetic loss-of-function models will be essential to distinguish the contributions of NOX enzymes versus mitochondria.

- **Integration of functional and physiological endpoints:** Beyond redox biomarkers, studies should incorporate physiological outcomes relevant to exercise performance and health. This includes acute and chronic assessments of ventilatory and cardiovascular responses, inflammatory biomarkers, skeletal muscle blood flow, and endurance capacity. Linking redox alterations with functional impairments will enhance translational relevance.
- **Consideration of potential co-pollutant interactions and local factors:** In urban environments, multiple air pollutants coexist and may act synergistically or antagonistically to influence the effects of exercise. The primary sources of PM and gaseous pollutants at the exposure site should be systematically characterized and reported. Given the heterogeneous and context-specific nature of air pollution, locally conducted studies are encouraged to provide more direct benefits to the surrounding community. Seasonal and regional variability in pollutant levels, along with methodological factors, should also be considered.
- **Communication and outreach:** Effective dissemination of research findings is essential to bridge the gap between scientific advances and public health practice. Results should be communicated not only to the scientific community but also to policymakers, healthcare providers, and the general public in clear and accessible language. Collaboration with local authorities can enhance awareness of air pollution risks and promote evidence-based exercise recommendations. Outreach strategies should also consider vulnerable groups, such as children, the elderly, and patients with cardiometabolic or respiratory conditions, ensuring that messages are tailored and culturally relevant.

6. Conclusions

Physical exercise and air pollution exert opposing effects on redox biology: while adequate physical activity induces transient, compartmentalized ROS that promote beneficial adaptations, air pollution generates sustained oxidative stress that contributes to inflammation and disease. These contrasting redox signals converge on shared pathways, including NOX isoforms, Nrf2, PRDX2, and mitochondria, which can mediate either adaptive or detrimental outcomes depending on the context. Notably, how this redox tension impacts individuals with pre-existing respiratory or cardiovascular conditions, who are both particularly susceptible to air pollution effects and recommended to engage in regular exercise, remains unclear. Furthermore, it is poorly explored how other environmental stressors that are highly prevalent in urban areas may further influence physiological responses to exercise.

Emerging evidence suggests that pollutant exposure during exercise may dampen its health benefits or even exacerbate harm, particularly in individuals exposed to high levels of $PM_{2.5}$. However, the direction and magnitude of these effects are influenced by exercise intensity, pollutant type, age, and individual fitness. In this regard, high-quality and updated information from local public agencies on air quality is critical for proper advice on when best to exercise outdoors or stay indoors. Future research should focus on identifying redox thresholds for adaptation versus dysfunction, standardizing experimental models, and informing public health strategies to preserve the benefits of exercise in polluted environments.

CRediT authorship contribution statement

Valentina Jeria-Espinoza: Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **Carlos Henriquez-Olguin:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization. **Edgardo Opazo-Diaz:** Writing – original draft, Investigation. **Timoteo Marchini:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used ChatGPT to identify grammar and typographical issues. The authors subsequently reviewed and edited the content as needed and take full responsibility for the final version of the manuscript.

Conflicts of interest

The authors have no conflicting interests to disclose.

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References

[1] O. Hahad, A. Daiber, T. Munzel, Physical activity in polluted air: an urgent call to study the health risks, Lancet Planet. Health 7 (4) (2023) e266–e267.
[2] J. Lelieveld, K. Klingmuller, A. Pozzer, U. Poschl, M. Fnais, A. Daiber, T. Munzel, Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions, Eur. Heart J. 40 (20) (2019) 1590–1596.
[3] S.G. Al-Kindi, R.D. Brook, S. Biswal, S. Rajagopalan, Environmental determinants of cardiovascular disease: lessons learned from air pollution, Nat. Rev. Cardiol. 17 (10) (2020) 656–672.
[4] Y.Y. Xu, J. Xie, H. Yin, F.F. Yang, C.M. Ma, B.Y. Yang, R. Wan, B. Guo, L.D. Chen, S.L. Li, The global burden of disease attributable to low physical activity and its trends from 1990 to 2019: an analysis of the global burden of disease study, Front. Public Health 10 (2022) 1018866.
[5] R. Fuller, P.J. Landrigan, K. Balakrishnan, G. Bathan, S. Bose-O'Reilly, M. Brauer, J. Caravanos, T. Chiles, A. Cohen, L. Corra, M. Cropper, G. Ferraro, J. Hanna, D. Hanrahan, H. Hu, D. Hunter, G. Janata, R. Kupka, B. Lanphear, M. Lichtveld, K. Martin, A. Mustapha, E. Sanchez-Triana, K. Sandilya, L. Schaefli, J. Shaw, J. Seddon, W. Suk, M.M. Tellez-Rojo, C. Yan, Pollution and health: a progress update, Lancet Planet. Health 6 (6) (2022) e535–e547.
[6] B.K. Pedersen, B. Saltin, Evidence for prescribing exercise as therapy in chronic disease, Scand. J. Med. Sci. Sports 16 (Suppl 1) (2006) 3–63.
[7] C. Henriquez-Olguin, R. Meneses-Valdes, P. Kritsiligkou, E. Fuentes-Lemus, From workout to molecular switches: how does skeletal muscle produce, sense, and transduce subcellular redox signals? Free Radic. Biol. Med. 209 (Pt 2) (2023) 355–365.
[8] S.K. Powers, J. Duarte, A.N. Kavazis, E.E. Talbert, Reactive oxygen species are signalling molecules for skeletal muscle adaptation, Exp. Physiol. 95 (1) (2010) 1–9.
[9] N.A. Strobel, J.M. Peake, A. Matsumoto, S.A. Marsh, J.S. Coombes, G.D. Wadley, Antioxidant supplementation reduces skeletal muscle mitochondrial biogenesis, Med. Sci. Sports Exerc. 43 (6) (2011) 1017–1024.
[10] M.C. Gomez-Cabrera, E. Domenech, J. Vina, Moderate exercise is an antioxidant: upregulation of antioxidant genes by training, Free Radic. Biol. Med. 44 (2) (2008) 126–131.
[11] M. Ristow, K. Zarse, A. Oberbach, N. Kloting, M. Birringer, M. Kiehntopf, M. Stumvoll, C.R. Kahn, M. Bluher, Antioxidants prevent health-promoting effects of physical exercise in humans, Proc. Natl. Acad. Sci. U. S. A. 106 (21) (2009) 8665–8670.
[12] T. Marchini, A. Zirlik, D. Wolf, Pathogenic role of air pollution particulate matter in cardiometabolic disease: evidence from mice and humans, Antioxidants Redox Signal. 33 (4) (2020) 263–279.
[13] S. Rajagopalan, S.G. Al-Kindi, R.D. Brook, Air pollution and cardiovascular disease: JACC state-of-the-art review, J. Am. Coll. Cardiol. 72 (17) (2018) 2054–2070.

[14] W. Li, W. Luo, S. Guo, Y. Yang, J. Yi, C. Li, G. Shen, H. Gao, Fine particulate matter, physical activity and cardiovascular disease in middle-aged and older Chinese adults, BMJ Open Sport Exerc Med. 11 (3) (2025) e002358.
[15] L. Martin, H. Nasir, R. Bagheri, U.C. Ugbolue, C. Laporte, J.S. Baker, Y. Gu, M. Zak, M. Duclos, F. Dutheil, Physical activity, air pollution, and mortality: a systematic review and meta-analysis, Sports Med. Open 11 (1) (2025) 35.
[16] D. Sun, C. Liu, Y. Ding, C. Yu, Y. Guo, D. Sun, Y. Pang, P. Pei, H. Du, L. Yang, Y. Chen, X. Meng, Y. Liu, J. Liu, R. Sohoni, G. Sansome, J. Chen, Z. Chen, J. Lv, H. Kan, L. Li, G. China, Kadoorie biobank collaborative, long-term exposure to ambient PM(2.5), active commuting, and farming activity and cardiovascular disease risk in adults in China: a prospective cohort study, Lancet Planet. Health 7 (4) (2023) e304–e312.
[17] M.P. Murphy, H. Bayir, V. Belousov, C.J. Chang, K.J.A. Davies, M.J. Davies, T. P. Dick, T. Finkel, H.J. Forman, Y. Janssen-Heininger, D. Gems, V.E. Kagan, B. Kalyanaraman, N.G. Larsson, G.L. Milne, T. Nystrom, H.E. Poulsen, R. Radi, H. Van Remmen, P.T. Schumacker, P.J. Thornalley, S. Toyokuni, C. C. Winterbourn, H. Yin, B. Halliwell, Guidelines for measuring reactive oxygen species and oxidative damage in cells and in vivo, Nat. Metab. 4 (6) (2022) 651–662.
[18] C.C. Winterbourn, Reconciling the chemistry and biology of reactive oxygen species, Nat. Chem. Biol. 4 (5) (2008) 278–286.
[19] K.J. Davies, A.T. Quintanilha, G.A. Brooks, L. Packer, Free radicals and tissue damage produced by exercise, Biochem. Biophys. Res. Commun. 107 (4) (1982) 1198–1205.
[20] M.J. Jackson, R.H. Edwards, M.C. Symons, Electron spin resonance studies of intact mammalian skeletal muscle, Biochim. Biophys. Acta 847 (2) (1985) 185–190.
[21] H. Sies, V.V. Belousov, N.S. Chandel, M.J. Davies, D.P. Jones, G.E. Mann, M. P. Murphy, M. Yamamoto, C. Winterbourn, Defining roles of specific reactive oxygen species (ROS) in cell biology and physiology, Nat. Rev. Mol. Cell Biol. 23 (7) (2022) 499–515.
[22] M.C. Gomez-Cabrera, E. Domenech, M. Romagnoli, A. Arduini, C. Borras, F. V. Pallardo, J. Sastre, J. Vina, Oral administration of vitamin C decreases muscle mitochondrial biogenesis and hampers training-induced adaptations in endurance performance, Am. J. Clin. Nutr. 87 (1) (2008) 142–149.
[23] D. Morrison, J. Hughes, P.A. Della Gatta, S. Mason, S. Lamon, A.P. Russell, G. D. Wadley, Vitamin C and E supplementation prevents some of the cellular adaptations to endurance-training in humans, Free Radic. Biol. Med. 89 (2015) 852–862.
[24] S.K. Powers, Z. Radak, L.L. Ji, M. Jackson, Reactive oxygen species promote endurance exercise-induced adaptations in skeletal muscles, J. Sport Health Sci. 13 (6) (2024) 780–792.
[25] C. Henriquez-Olguin, J.R. Knudsen, S.H. Raun, Z. Li, E. Dalbram, J.T. Treebak, L. Sylow, R. Holmdahl, E.A. Richter, E. Jaimovich, T.E. Jensen, Cytosolic ROS production by NADPH oxidase 2 regulates muscle glucose uptake during exercise, Nat. Commun. 10 (1) (2019) 4623.
[26] C. Henriquez-Olguin, L.B. Renani, L. Arab-Ceschia, S.H. Raun, A. Bhatia, Z. Li, J. R. Knudsen, R. Holmdahl, T.E. Jensen, Adaptations to high-intensity interval training in skeletal muscle require NADPH oxidase 2, Redox Biol. 24 (2019) 101188.
[27] R. Kano, T. Kusano, R. Takeda, H. Shirakawa, D.C. Poole, Y. Kano, D. Hoshino, Eccentric contraction increases hydrogen peroxide levels and alters gene expression through Nox2 in skeletal muscle of male mice, J. Appl. Physiol. 137 (3) (2024) 778–788, 1985.
[28] C. Henriquez-Olguin, A. Diaz-Vegas, Y. Utreras-Mendoza, C. Campos, M. Arias-Calderon, P. Llanos, A. Contreras-Ferrat, A. Espinosa, F. Altamirano, E. Jaimovich, D.M. Valladares, NOX2 inhibition impairs early muscle gene expression induced by a single exercise bout, Front. Physiol. 7 (2016) 282.
[29] C.E. Xirouchaki, Y. Jia, M.J. McGrath, S. Greatorex, M. Tran, T.L. Merry, D. Hong, M.J. Eramo, S.C. Broome, J.S.T. Woodhead, F. D'Souza R, J. Gallagher, E. Salimova, C. Huang, R.B. Schittenhelm, J. Sadoshima, M.J. Watt, C.A. Mitchell, T. Tiganis, Skeletal muscle NOX4 is required for adaptive responses that prevent insulin resistance, Sci. Adv. 7 (51) (2021) eabl4988.
[30] D.P. Jones, H. Sies, The redox code, Antioxidants Redox Signal. 23 (9) (2015) 734–746.
[31] S. Garcia-Santamarina, S. Boronat, E. Hidalgo, Reversible cysteine oxidation in hydrogen peroxide sensing and signal transduction, Biochemistry 53 (16) (2014) 2560–2580.
[32] J.V. Cross, D.J. Templeton, Regulation of signal transduction through protein cysteine oxidation, Antioxidants Redox Signal. 8 (9–10) (2006) 1819–1827.
[33] J. Bolduc, K. Koruza, T. Luo, J. Malo Pueyo, T.N. Vo, D. Ezerina, J. Messens, Peroxiredoxins wear many hats: factors that fashion their peroxide sensing personalities, Redox Biol. 42 (2021) 101959.
[34] A.V. Peskin, C.C. Winterbourn, The enigma of 2-Cys peroxiredoxins: what are their roles? Biochemistry (Mosc) 86 (1) (2021) 84–91.
[35] R.A. Heaton, S.T. Ball, C.A. Staunton, V. Mouly, S.W. Jones, A. McArdle, M. J. Jackson, Peroxiredoxin 2 mediates redox-stimulated adaptations to oxidative phosphorylation induced by contractile activity in human skeletal muscle myotubes, Free Radic. Biol. Med. 227 (2025) 395–406.
[36] C. Stretton, J.N. Pugh, B. McDonagh, A. McArdle, G.L. Close, M.J. Jackson, 2-Cys peroxiredoxin oxidation in response to hydrogen peroxide and contractile activity in skeletal muscle: a novel insight into exercise-induced redox signalling? Free Radic. Biol. Med. 160 (2020) 199–207.
[37] Q. Xia, J.C. Casas-Martinez, E. Zarzuela, J. Munoz, A. Miranda-Vizuete, K. Goljanek-Whysall, B. McDonagh, Peroxiredoxin 2 is required for the redox mediated adaptation to exercise, Redox Biol. 60 (2023) 102631.
[38] Q. Xia, P. Li, J.C. Casas-Martinez, A. Miranda-Vizuete, E. McDermott, P. Dockery, K. Goljanek-Whysall, B. McDonagh, Peroxiredoxin 2 regulates DAF-16/FOXO mediated mitochondrial remodelling in response to exercise that is disrupted in ageing, Mol. Metabol. 88 (2024) 102003.
[39] F.J. Kelly, J.C. Fussell, Size, source and chemical composition as determinants of toxicity attributable to ambient particulate matter, Atmos. Environ. 60 (2012) 504–526.
[40] V.A. Southerland, M. Brauer, A. Mohegh, M.S. Hammer, A. van Donkelaar, R. V. Martin, J.S. Apte, S.C. Anenberg, Global urban temporal trends in fine particulate matter (PM(2.5)) and attributable health burdens: estimates from global datasets, Lancet Planet. Health 6 (2) (2022) e139–e146.
[41] W. Yu, T. Ye, Y. Zhang, R. Xu, Y. Lei, Z. Chen, Z. Yang, Y. Zhang, J. Song, X. Yue, S. Li, Y. Guo, Global estimates of daily ambient fine particulate matter concentrations and unequal spatiotemporal distribution of population exposure: a machine learning modelling study, Lancet Planet. Health 7 (3) (2023) e209–e218.
[42] K.R. Daellenbach, G. Uzu, J. Jiang, L.E. Cassagnes, Z. Leni, A. Vlachou, G. Stefenelli, F. Canonaco, S. Weber, A. Segers, J.J.P. Kuenen, M. Schaap, O. Favez, A. Albinet, S. Aksoyoglu, J. Dommen, U. Baltensperger, M. Geiser, I. El Haddad, J.L. Jaffrezo, A.S.H. Prevot, Sources of particulate-matter air pollution and its oxidative potential in Europe, Nature 587 (7834) (2020) 414–419.
[43] G. Valacchi, N. Magnani, B. Woodby, S.M. Ferreira, P. Evelson, Particulate matter induces tissue OxInflammation: from mechanism to damage, Antioxidants Redox Signal. 33 (4) (2020) 308–326.
[44] G. Valacchi, F. Virgili, C. Cervellati, A. Pecorelli, OxInflammation: from subclinical condition to pathological biomarker, Front. Physiol. 9 (2018) 858.
[45] R. DeVries, D. Kriebel, S. Sama, Outdoor air pollution and COPD-related emergency department visits, hospital admissions, and mortality: a meta-analysis, COPD J. Chronic Obstr. Pulm. Dis. 14 (1) (2017) 113–121.
[46] W. Hill, E.L. Lim, C.E. Weeden, C. Lee, M. Augustine, K. Chen, F.C. Kuan, F. Marongiu, E.J. Evans Jr., D.A. Moore, F.S. Rodrigues, O. Pich, B. Bakker, H. Cha, R. Myers, F. van Maldegem, J. Boumelha, S. Veeriah, A. Rowan, C. Naceur-Lombardelli, T. Karasaki, M. Sivakumar, S. De, D.R. Caswell, A. Nagano, J.R.M. Black, C. Martinez-Ruiz, M.H. Ryu, R.D. Huff, S. Li, M.J. Fave, A. Magness, A. Suarez-Bonnet, S.L. Priestnall, M. Luchtenborg, K. Lavelle, J. Pethick, S. Hardy, F.E. McRonald, M.H. Lin, C.I. Troccoli, M. Ghosh, Y.E. Miller, D.T. Merrick, R.L. Keith, M. Al Bakir, C. Bailey, M.S. Hill, L.H. Saal, Y. Chen, A. M. George, C. Abbosh, N. Kanu, S.H. Lee, N. McGranahan, C.D. Berg, P. Sasieni, R. Houlston, C. Turnbull, S. Lam, P. Awadalla, E. Gronroos, J. Downward, T. Jacks, C. Carlsten, I. Malanchi, A. Hackshaw, K. Litchfield, T.R. Consortium, J. DeGregori, M. Jamal-Hanjani, C. Swanton, Lung adenocarcinoma promotion by air pollutants, Nature 616 (7955) (2023) 159–167.
[47] S.A. Gurgueira, J. Lawrence, B. Coull, G.G. Murthy, B. Gonzalez-Flecha, Rapid increases in the steady-state concentration of reactive oxygen species in the lungs and heart after particulate air pollution inhalation, Environ. Health Perspect. 110 (8) (2002) 749–755.
[48] J. Lelieveld, A. Pozzer, U. Poschl, M. Fnais, A. Haines, T. Munzel, Loss of life expectancy from air pollution compared to other risk factors: a worldwide perspective, Cardiovasc. Res. 116 (11) (2020) 1910–1917.
[49] O. Hahad, J. Lelieveld, F. Birklein, K. Lieb, A. Daiber, T. Munzel, Ambient air pollution increases the risk of cerebrovascular and neuropsychiatric disorders through induction of inflammation and oxidative stress, Int. J. Mol. Sci. 21 (12) (2020).
[50] J.T. Bates, T. Fang, V. Verma, L. Zeng, R.J. Weber, P.E. Tolbert, J.Y. Abrams, S. E. Sarnat, M. Klein, J.A. Mulholland, A.G. Russell, Review of acellular assays of ambient particulate matter oxidative potential: methods and relationships with composition, sources, and health effects, Environ. Sci. Technol. 53 (8) (2019) 4003–4019.
[51] H.J. Forman, C.E. Finch, A critical review of assays for hazardous components of air pollution, Free Radic. Biol. Med. 117 (2018) 202–217.
[52] G.D. Thurston, R.T. Burnett, M.C. Turner, Y. Shi, D. Krewski, R. Lall, K. Ito, M. Jerrett, S.M. Gapstur, W.R. Diver, C.A. Pope, Ischemic heart disease mortality and long-term exposure to source-related components of U.S. fine particle air pollution, Environ. Health Perspect. 124 (6) (2016) 785–794.
[53] S. Weichenthal, L.L. Pinault, R.T. Burnett, Impact of oxidant gases on the relationship between outdoor fine particulate air pollution and nonaccidental, cardiovascular, and respiratory mortality, Sci. Rep. 7 (1) (2017) 16401.
[54] Q. Di, L. Dai, Y. Wang, A. Zanobetti, C. Choirat, J.D. Schwartz, F. Dominici, Association of short-term exposure to air pollution with mortality in older adults, JAMA 318 (24) (2017) 2446–2456.
[55] Y. Niu, Y. Zhou, R. Chen, P. Yin, X. Meng, W. Wang, C. Liu, J.S. Ji, Y. Qiu, H. Kan, M. Zhou, Long-term exposure to ozone and cardiovascular mortality in China: a nationwide cohort study, Lancet Planet. Health 6 (6) (2022) e496–e503.
[56] X. Xia, X. Meng, C. Liu, Y. Guo, X. Li, Y. Niu, K.B.H. Lam, N. Wright, C. Kartsonaki, Y. Chen, L. Yang, H. Du, C. Yu, D. Sun, J. Lv, J. Chen, X. Yang, R. Gao, S. Wu, H. Kan, K.H. Chan, L. Li, Z. Chen, G. China Kadoorie Biobank Study, Associations of long-term nitrogen dioxide exposure with a wide spectrum of diseases: a prospective cohort study of 0.5 million Chinese adults, Lancet Public Health 9 (12) (2024) e1047–e1058.
[57] T. Munzel, M. Sorensen, J. Lelieveld, P.J. Landrigan, M. Kuntic, M. Nieuwenhuijsen, M.R. Miller, A. Schneider, A. Daiber, A comprehensive review/expert statement on environmental risk factors of cardiovascular disease, Cardiovasc. Res. (2025). https://pubmed.ncbi.nlm.nih.gov/40795898.
[58] T. Munzel, M. Sorensen, J. Lelieveld, O. Hahad, S. Al-Kindi, M. Nieuwenhuijsen, B. Giles-Corti, A. Daiber, S. Rajagopalan, Heart healthy cities: genetics loads the gun but the environment pulls the trigger, Eur. Heart J. 42 (25) (2021) 2422–2438.

[59] J. Lelieveld, J.S. Evans, M. Fnais, D. Giannadaki, A. Pozzer, The contribution of outdoor air pollution sources to premature mortality on a global scale, Nature 525 (7569) (2015) 367–371.
[60] K. Wolf, B. Hoffmann, Z.J. Andersen, R.W. Atkinson, M. Bauwelinck, T. Bellander, J. Brandt, B. Brunekreef, G. Cesaroni, J. Chen, U. de Faire, K. de Hoogh, D. Fecht, F. Forastiere, J. Gulliver, O. Hertel, U.A. Hvidtfeldt, N.A.H. Janssen, J. T. Jorgensen, K. Katsouyanni, M. Ketzel, J.O. Klompmaker, A. Lager, S. Liu, C. J. MacDonald, P.K.E. Magnusson, A.J. Mehta, G. Nagel, B. Oftedal, N.L. Pedersen, G. Pershagen, O. Raaschou-Nielsen, M. Renzi, D. Rizzuto, S. Rodopoulou, E. Samoli, Y.T. van der Schouw, S. Schramm, P. Schwarze, T. Sigsgaard, M. Sorensen, M. Stafoggia, M. Strak, A. Tjonneland, W.M.M. Verschuren, D. Vienneau, G. Weinmayr, G. Hoek, A. Peters, P.L.S. Ljungman, Long-term exposure to low-level ambient air pollution and incidence of stroke and coronary heart disease: a pooled analysis of six European cohorts within the ELAPSE project, Lancet Planet. Health 5 (9) (2021) e620–e632.
[61] C. Liu, R. Chen, F. Sera, A.M. Vicedo-Cabrera, Y. Guo, S. Tong, E. Lavigne, P. M. Correa, N.V. Ortega, S. Achilleos, D. Roye, J.J. Jaakkola, N. Ryti, M. Pascal, A. Schneider, S. Breitner, A. Entezari, F. Mayvaneh, R. Raz, Y. Honda, M. Hashizume, C.F.S. Ng, V. Gaio, J. Madureira, I.H. Holobaca, A. Tobias, C. Iniguez, Y.L. Guo, S.C. Pan, P. Masselot, M.L. Bell, A. Zanobetti, J. Schwartz, A. Gasparrini, H. Kan, Interactive effects of ambient fine particulate matter and ozone on daily mortality in 372 cities: two stage time series analysis, BMJ 383 (2023) e075203.
[62] S. Rajagopalan, R.D. Brook, P. Salerno, B. Bourges-Sevenier, P. Landrigan, M. J. Nieuwenhuijsen, T. Munzel, S.V. Deo, S. Al-Kindi, Air pollution exposure and cardiometabolic risk, Lancet Diabetes Endocrinol. 12 (3) (2024) 196–208.
[63] M.R. Miller, Oxidative stress and the cardiovascular effects of air pollution, Free Radic. Biol. Med. 151 (2020) 69–87.
[64] T. Marchini, Redox and inflammatory mechanisms linking air pollution particulate matter with cardiometabolic derangements, Free Radic. Biol. Med. 209 (Pt 2) (2023) 320–341.
[65] S. Soberanes, A.V. Misharin, A. Jairaman, L. Morales-Nebreda, A.C. McQuattie-Pimentel, T. Cho, R.B. Hamanaka, A.Y. Meliton, P.A. Reyfman, J.M. Walter, C. I. Chen, M. Chi, S. Chiu, F.J. Gonzalez-Gonzalez, M. Antalek, H. Abdala-Valencia, S.E. Chiarella, K.A. Sun, P.S. Woods, A.J. Ghio, M. Jain, H. Perlman, K.M. Ridge, R.I. Morimoto, J.I. Sznajder, W.E. Balch, S.M. Bhorade, A. Bharat, M. Prakriya, N. S. Chandel, G.M. Mutlu, G.R.S. Budinger, Metformin targets mitochondrial electron transport to reduce air-pollution-induced thrombosis, Cell Metab. 29 (2) (2019) 335–347 e5.
[66] L. Caceres, M.L. Paz, M. Garces, V. Calabro, N.D. Magnani, M. Martinefski, P. V. Martino Adami, L. Caltana, D. Tasat, L. Morelli, V. Tripodi, G. Valacchi, S. Alvarez, D. Gonzalez Maglio, T. Marchini, P. Evelson, NADPH oxidase and mitochondria are relevant sources of superoxide anion in the oxinflammatory response of macrophages exposed to airborne particulate matter, Ecotoxicol. Environ. Saf. 205 (2020) 111186.
[67] M. Pardo, X. Qiu, R. Zimmermann, Y. Rudich, Particulate matter toxicity is Nrf2 and mitochondria dependent: the roles of metals and polycyclic aromatic hydrocarbons, Chem. Res. Toxicol. 33 (5) (2020) 1110–1120.
[68] A. Shukla, C. Timblin, K. BeruBe, T. Gordon, W. McKinney, K. Driscoll, P. Vacek, B.T. Mossman, Inhaled particulate matter causes expression of nuclear factor (NF)-kappaB-related genes and oxidant-dependent NF-kappaB activation in vitro, Am. J. Respir. Cell Mol. Biol. 23 (2) (2000) 182–187.
[69] L. Caceres, T. Abogunloko, S. Malchow, F. Ehret, J. Merz, X. Li, L. Sol Mitre, N. Magnani, D. Tasat, T. Mwinyella, L. Spiga, D. Suchanek, L. Fischer, O. Gorka, M. Colin Gissler, I. Hilgendorf, P. Stachon, E. Rog-Zielinska, O. Gross, D. Westermann, P. Evelson, D. Wolf, T. Marchini, Molecular mechanisms underlying NLRP3 inflammasome activation and IL-1beta production in air pollution fine particulate matter (PM(2.5))-primed macrophages, Environ. Pollut. 341 (2024) 122997.
[70] T. Kampfrath, A. Maiseyeu, Z. Ying, Z. Shah, J.A. Deiuliis, X. Xu, N. Kherada, R. D. Brook, K.M. Reddy, N.P. Padture, S. Parthasarathy, L.C. Chen, S. Moffatt-Bruce, Q. Sun, H. Morawietz, S. Rajagopalan, Chronic fine particulate matter exposure induces systemic vascular dysfunction via NADPH oxidase and TLR4 pathways, Circ. Res. 108 (6) (2011) 716–726.
[71] C. Liu, L.K. Fonken, A. Wang, A. Maiseyeu, Y. Bai, T.Y. Wang, S. Maurya, Y.A. Ko, M. Periasamy, T. Dvonch, M. Morishita, R.D. Brook, J. Harkema, Z. Ying, B. Mukherjee, Q. Sun, R.J. Nelson, S. Rajagopalan, Central IKKbeta inhibition prevents air pollution mediated peripheral inflammation and exaggeration of type II diabetes, Part. Fibre Toxicol. 11 (2014) 53.
[72] J. Zhong, G. Zhao, S. Edwards, J. Tran, S. Rajagopalan, X. Rao, Particulate air pollution exaggerates diet-induced insulin resistance through NLRP3 inflammasome in mice, Environ. Pollut. 328 (2023) 121603.
[73] T. Marchini, N. Magnani, M. Garces, J. Kelly, M. Paz, L. Caceres, V. Calabro, R. Lasagni Vitar, L. Caltana, M. Contin, S. Reynoso, N. Lago, T. Vico, V. Vanasco, D. Wolf, V. Tripodi, D. Gonzalez Maglio, S. Alvarez, B. Buchholz, A. Berra, R. Gelpi, P. Evelson, Chronic exposure to polluted urban air aggravates myocardial infarction by impaired cardiac mitochondrial function and dynamics, Environ. Pollut. 295 (2022) 118677.
[74] C.A. Pope 3rd, A. Bhatnagar, J.P. McCracken, W. Abplanalp, D.J. Conklin, T. O'Toole, Exposure to fine particulate air pollution is associated with endothelial injury and systemic inflammation, Circ. Res. 119 (11) (2016) 1204–1214.
[75] Y. Lin, G. Ramanathan, Y. Zhu, F. Yin, N.D. Rea, X. Lu, C.H. Tseng, K.F. Faull, A. J. Yoon, M. Jerrett, T. Zhu, X. Qiu, J.A. Araujo, Pro-oxidative and proinflammatory effects after traveling from Los Angeles to Beijing: a biomarker-based natural experiment, Circulation 140 (24) (2019) 1995–2004.
[76] T.R. Nurkiewicz, D.W. Porter, M. Barger, L. Millecchia, K.M. Rao, P.J. Marvar, A. F. Hubbs, V. Castranova, M.A. Boegehold, Systemic microvascular dysfunction and inflammation after pulmonary particulate matter exposure, Environ. Health Perspect. 114 (3) (2006) 412–419.
[77] B.G. Hill, B. Rood, A. Ribble, P. Haberzettl, Fine particulate matter (PM(2.5)) inhalation-induced alterations in the plasma lipidome as promoters of vascular inflammation and insulin resistance, Am. J. Physiol. Heart Circ. Physiol. 320 (5) (2021) H1836–H1850.
[78] T.W. Cherng, M.L. Paffett, O. Jackson-Weaver, M.J. Campen, B.R. Walker, N. L. Kanagy, Mechanisms of diesel-induced endothelial nitric oxide synthase dysfunction in coronary arterioles, Environ. Health Perspect. 119 (1) (2011) 98–103.
[79] X. Xu, Z. Yavar, M. Verdin, Z. Ying, G. Mihai, T. Kampfrath, A. Wang, M. Zhong, M. Lippmann, L.C. Chen, S. Rajagopalan, Q. Sun, Effect of early particulate air pollution exposure on obesity in mice: role of p47phox, Arterioscler. Thromb. Vasc. Biol. 30 (12) (2010) 2518–2527.
[80] A. Daiber, M. Kuntic, O. Hahad, L.G. Delogu, S. Rohrbach, F. Di Lisa, R. Schulz, T. Munzel, Effects of air pollution particles (ultrafine and fine particulate matter) on mitochondrial function and oxidative stress - implications for cardiovascular and neurodegenerative diseases, Arch. Biochem. Biophys. 696 (2020) 108662.
[81] T. Marchini, N. Magnani, V. D'Annunzio, D. Tasat, R.J. Gelpi, S. Alvarez, P. Evelson, Impaired cardiac mitochondrial function and contractile reserve following an acute exposure to environmental particulate matter, Biochim. Biophys. Acta 1830 (3) (2013) 2545–2552.
[82] H. Wang, X. Shen, G. Tian, X. Shi, W. Huang, Y. Wu, L. Sun, C. Peng, S. Liu, Y. Huang, X. Chen, F. Zhang, Y. Chen, W. Ding, Z. Lu, AMPKalpha2 deficiency exacerbates long-term PM(2.5) exposure-induced lung injury and cardiac dysfunction, Free Radic. Biol. Med. 121 (2018) 202–214.
[83] G. Qin, J. Xia, Y. Zhang, L. Guo, R. Chen, N. Sang, Ambient fine particulate matter exposure induces reversible cardiac dysfunction and fibrosis in juvenile and older female mice, Part. Fibre Toxicol. 15 (1) (2018) 27.
[84] T. Marchini, D. Wolf, N.A. Michel, M. Mauler, B. Dufner, N. Hoppe, J. Beckert, M. Jackel, N. Magnani, D. Duerschmied, D. Tasat, S. Alvarez, J. Reinohl, C. von Zur Muhlen, M. Idzko, C. Bode, I. Hilgendorf, P. Evelson, A. Zirlik, Acute exposure to air pollution particulate matter aggravates experimental myocardial infarction in mice by potentiating cytokine secretion from lung macrophages, Basic Res. Cardiol. 111 (4) (2016) 44.
[85] W. Yue, L. Tong, X. Liu, X. Weng, X. Chen, D. Wang, S.C. Dudley, E.K. Weir, W. Ding, Z. Lu, Y. Xu, Y. Chen, Short term Pm2.5 exposure caused a robust lung inflammation, vascular remodeling, and exacerbated transition from left ventricular failure to right ventricular hypertrophy, Redox Biol. 22 (2019) 101161.
[86] Z. Xu, X. Xu, M. Zhong, I.P. Hotchkiss, R.P. Lewandowski, J.G. Wagner, L. A. Bramble, Y. Yang, A. Wang, J.R. Harkema, M. Lippmann, S. Rajagopalan, L. C. Chen, Q. Sun, Ambient particulate air pollution induces oxidative stress and alterations of mitochondria and gene expression in brown and white adipose tissues, Part. Fibre Toxicol. 8 (2011) 20.
[87] Q. Sun, P. Yue, J.A. Deiuliis, C.N. Lumeng, T. Kampfrath, M.B. Mikolaj, Y. Cai, M. C. Ostrowski, B. Lu, S. Parthasarathy, R.D. Brook, S.D. Moffatt-Bruce, L.C. Chen, S. Rajagopalan, Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity, Circulation 119 (4) (2009) 538–546.
[88] S. Rajagopalan, B. Park, R. Palanivel, V. Vinayachandran, J.A. Deiuliis, R. S. Gangwar, L. Das, J. Yin, Y. Choi, S. Al-Kindi, M.K. Jain, K.D. Hansen, S. Biswal, Metabolic effects of air pollution exposure and reversibility, J. Clin. Investig. 130 (11) (2020) 6034–6040.
[89] WHO, Physical activity. https://www.who.int/news-room/fact-sheets/detail/physical-activity, 2024. September 2025.
[90] C. Lundby, D. Montero, M. Joyner, Biology of VO(2) max: looking under the physiology lamp, Acta Physiol. 220 (2) (2017) 218–228.
[91] C. Fiuza-Luces, N. Garatachea, N.A. Berger, A. Lucia, Exercise is the real polypill, Physiology 28 (5) (2013) 330–358.
[92] O. Hahad, M. Kuntic, K. Frenis, S. Chowdhury, J. Lelieveld, K. Lieb, A. Daiber, T. Munzel, Physical activity in polluted air-net benefit or harm to cardiovascular health? A comprehensive review, Antioxidants 10 (11) (2021).
[93] W. Raza, B. Krachler, B. Forsberg, J.N. Sommar, Air pollution, physical activity and ischaemic heart disease: a prospective cohort study of interaction effects, BMJ Open 11 (4) (2021) e040912.
[94] W. Raza, B. Krachler, B. Forsberg, J.N. Sommar, Does physical activity modify the association between air pollution and recurrence of cardiovascular disease? Int .J. Environ. Res. Public Health 18 (5) (2021).
[95] S. Sun, W. Cao, H. Qiu, J. Ran, H. Lin, C. Shen, R. Siu-Yin Lee, L. Tian, Benefits of physical activity not affected by air pollution: a prospective cohort study, Int. J. Epidemiol. 49 (1) (2020) 142–152.
[96] S.R. Kim, D. Choi, S. Choi, K. Kim, G. Lee, J.S. Son, K.H. Kim, S.M. Park, Association of combined effects of physical activity and air pollution with diabetes in older adults, Environ. Int. 145 (2020) 106161.
[97] C. Guo, H.T. Yang, L.Y. Chang, Y. Bo, C. Lin, Y. Zeng, T. Tam, A.K.H. Lau, G. Hoek, X.Q. Lao, Habitual exercise is associated with reduced risk of diabetes regardless of air pollution: a longitudinal cohort study, Diabetologia 64 (6) (2021) 1298–1308.
[98] P.B. Dominelli, A.W. Sheel, The pulmonary physiology of exercise, Adv. Physiol. Educ. 48 (2) (2024) 238–251.
[99] K. Oravisjarvi, M. Pietikainen, J. Ruuskanen, A. Rautio, A. Voutilainen, R. L. Keiski, Effects of physical activity on the deposition of traffic-related particles into the human lungs in silico, Sci. Total Environ. 409 (21) (2011) 4511–4518.

[100] C.A. Cole, C. Carlsten, M. Koehle, M. Brauer, Particulate matter exposure and health impacts of urban cyclists: a randomized crossover study, Environ. Health 17 (1) (2018) 78.
[101] Q. Deng, C. Ou, Y.M. Shen, Y. Xiang, Y. Miao, Y. Li, Health effects of physical activity as predicted by particle deposition in the human respiratory tract, Sci. Total Environ. 657 (2019) 819–826.
[102] W.D. Bennett, M.S. Messina, G.C. Smaldone, Effect of exercise on deposition and subsequent retention of inhaled particles, J. Appl. Physiol. 59 (4) (1985) 1046–1054, 1985.
[103] G. Oberdorster, E. Oberdorster, J. Oberdorster, Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles, Environ. Health Perspect. 113 (7) (2005) 823–839.
[104] K.W. Rundell, J.B. Slee, R. Caviston, A.M. Hollenbach, Decreased lung function after inhalation of ultrafine and fine particulate matter during exercise is related to decreased total nitrate in exhaled breath condensate, Inhal. Toxicol. 20 (1) (2008) 1–9.
[105] A.J. Ghio, C. Kim, R.B. Devlin, Concentrated ambient air particles induce mild pulmonary inflammation in healthy human volunteers, Am. J. Respir. Crit. Care Med. 162 (3 Pt 1) (2000) 981–988.
[106] B.M. Larsson, M. Sehlstedt, J. Grunewald, C.M. Skold, A. Lundin, A. Blomberg, T. Sandstrom, A. Eklund, M. Svartengren, Road tunnel air pollution induces bronchoalveolar inflammation in healthy subjects, Eur. Respir. J. 29 (4) (2007) 699–705.
[107] L. Jacobs, T.S. Nawrot, B. de Geus, R. Meeusen, B. Degraeuwe, A. Bernard, M. Sughis, B. Nemery, L.I. Panis, Subclinical responses in healthy cyclists briefly exposed to traffic-related air pollution: an intervention study, Environ. Health 9 (2010) 64.
[108] D. Stieb, R.H. Shutt, L.M. Kauri, S. Mason-Renton, L. Chen, M. Szyszkowicz, N. A. Dobbin, M. Rigden, B. Jovic, M. Mulholland, M.S. Green, L. Liu, G. Pelletier, S. A. Weichenthal, R.E. Dales, J. Andrade, I. Luginaah, Associations between air pollution and cardio-respiratory physiological measures in older adults exercising outdoors, Int. J. Environ. Health Res. 31 (8) (2021) 901–914.
[109] A.P. Pietropaoli, M.W. Frampton, R.W. Hyde, P.E. Morrow, G. Oberdorster, C. Cox, D.M. Speers, L.M. Frasier, D.C. Chalupa, L.S. Huang, M.J. Utell, Pulmonary function, diffusing capacity, and inflammation in healthy and asthmatic subjects exposed to ultrafine particles, Inhal. Toxicol. 16 (Suppl 1) (2004) 59–72.
[110] N.J. Kubesch, A. de Nazelle, D. Westerdahl, D. Martinez, G. Carrasco-Turigas, L. Bouso, S. Guerra, M.J. Nieuwenhuijsen, Respiratory and inflammatory responses to short-term exposure to traffic-related air pollution with and without moderate physical activity, Occup. Environ. Med. 72 (4) (2015) 284–293.
[111] J.R. Balmes, M. Arjomandi, P.A. Bromberg, M.G. Costantini, N. Dagincourt, M. J. Hazucha, D. Hollenbeck-Pringle, D.Q. Rich, P. Stark, M.W. Frampton, Ozone effects on blood biomarkers of systemic inflammation, oxidative stress, endothelial function, and thrombosis: the multicenter ozone study in oldEr subjects (MOSES), PLoS One 14 (9) (2019) e0222601.
[112] L.C. Avila, T.R. Bruggemann, F. Bobinski, M.D. da Silva, R.C. Oliveira, D. F. Martins, L. Mazzardo-Martins, M.M. Duarte, L.F. de Souza, A. Dafre, R. P. Vieira, A.R. Santos, K.C. Bonorino, D.C. Hizume Kunzler, Effects of high-intensity swimming on lung inflammation and oxidative stress in a murine model of DEP-induced injury, PLoS One 10 (9) (2015) e0137273.
[113] D. Fan, K. Pan, J. Guo, Z. Liu, C. Zhang, J. Zhang, X. Qian, H. Shen, J. Zhao, Exercise ameliorates fine particulate matter-induced metabolic damage through the SIRT1/AMPKalpha/PGC1-alpha/NRF1 signaling pathway, Environ. Res. 245 (2024) 117973.
[114] B. Feng, R. Qi, J. Gao, T. Wang, H. Xu, Q. Zhao, R. Wu, X. Song, J. Guo, L. Zheng, R. Li, W. Huang, Exercise training prevented endothelium dysfunction from particulate matter instillation in Wistar rats, Sci. Total Environ. 694 (2019) 133674.
[115] A.S. Mai, A.B. Dos Santos, L.C.C. Beber, R.D.B. Basso, L.M. Sulzbacher, P. B. Goettems-Fiorin, M.N. Frizzo, C.R. Rhoden, M.S. Ludwig, T.G. Heck, Exercise training under exposure to low levels of fine particulate matter: effects on heart oxidative stress and extra-to-intracellular HSP70 ratio, Oxid. Med. Cell. Longev. 2017 (2017) 9067875.
[116] S.Y. Cho, H.T. Roh, Impact of particulate matter exposure and aerobic exercise on circulating biomarkers of oxidative stress, antioxidant status, and inflammation in young and aged mice, Life (Basel) 13 (10) (2023).
[117] J.W. Illing, F.J. Miller, D.E. Gardner, Decreased resistance to infection in exercised mice exposed to NO2 and O3, J. Toxicol. Environ. Health 6 (4) (1980) 843–851.
[118] D.K. Bhalla, R.C. Mannix, S.M. Lavan, R.F. Phalen, M.T. Kleinman, T.T. Crocker, Tracheal and bronchoalveolar permeability changes in rats inhaling oxidant atmospheres during rest or exercise, J. Toxicol. Environ. Health 22 (4) (1987) 417–437.
[119] N.C. Long, J. Suh, J.D. Morrow, R.H. Schiestl, G.G. Murthy, J.D. Brain, B. Frei, Ozone causes lipid peroxidation but little antioxidant depletion in exercising and nonexercising hamsters, J. Appl. Physiol. 91 (4) (2001) 1694–1700, 1985.
[120] J. Zhao, F. Gong, Q. Yang, R. Yang, Z. Yan, Z. Xi, K. Li, W. Lai, Y. Shi, B. Lin, J. Yan, X. Liu, Exercise in ozone-polluted air evokes pathological cardiac hypertrophy via up-regulation of nuclear lncRNA EYA4-au1 and recruiting Med11 to activating EYA4/p27kip1/CK2alpha/HDAC2 cascade, Ecotoxicol. Environ. Saf. 287 (2024) 117264.
[121] C.J. Gordon, P.M. Phillips, A. Ledbetter, S.J. Snow, M.C. Schladweiler, A. F. Johnstone, U.P. Kodavanti, Active vs. sedentary lifestyle from weaning to adulthood and susceptibility to ozone in rats, Am. J. Physiol. Lung Cell. Mol. Physiol. 312 (1) (2017) L100–L109.