



Special Issue "Impact of environmental pollution and stress on redox signaling and oxidative stress pathways"

Within the last decades, the global burden of disease (GBD) has shifted from communicable, maternal, perinatal, and nutritional causes to non-communicable diseases such as atherosclerosis or metabolic disease [1,2]. Genome-wide association studies aimed to identify the genetic risk factors underlying non-communicable diseases in order to explain their genetic (familial) predisposition in large populations. More recently, there was a change of this dogma due to the increasing evidence that genetic (familial) predisposition for non-communicable diseases may be outcompeted by environmental risk factors, also reflected by the statement of G.A. Bray "The genetic background loads the gun, but the environment pulls the trigger" [3], also put forward by F. Collins, the director of the NIH. Based on these recent scientific advances, a new research field was defined by the term "exposome" [4], which comprises the changes of our endogenous biochemical systems by life-long environmental/behavioral exposures and our social environment as well as the associated health effects [5,6].

There is increasing evidence that environmental stressors such as air pollution, noise and mental stress may facilitate the development of chronic non-communicable disease [7,8]. Recent reports of the Lancet Commission on Pollution and Health [9], the World Health Organization [10] and the Global Burden of Disease Study [11,12] reported that environmental risk factors significantly contribute to the global burden of disease. All forms of pollution together caused 9 to 12.6 million deaths in 2015 and 2012 [9,10], respectively, reflecting 16–20% of total mortality worldwide and representing a higher number of annual deaths than estimated for smoking. These numbers will rather increase than decrease since most recent mathematical models using geographic pollution and health data predict almost 9 million deaths attributable to air pollution alone [13,14]. Of note, air pollution was identified as the leading health risk factor in the physical environment, followed by water/soil pollution and occupational exposures by (in)organic particles, heavy metals, pesticides and other chemicals [9], however neglecting the non-chemical environmental health risk factors mental stress, noise, light exposure and climatic changes. Epidemiological data suggest that environmental risk factors are associated with higher risk for cardiovascular, metabolic and mental disease including hypertension, heart failure, myocardial infarction, diabetes, arrhythmia, stroke, neurodegeneration, depression and anxiety disorders (e.g. for noise see Refs. [15,16]). The mechanisms underlying environmentally triggered non-communicable disease are not fully understood but may comprise increased stress hormone release (cortisol, adrenaline, noradrenaline), oxidative stress and inflammation leading to adverse health effects.

With the present Special Issue, we want to highlight the redox biology and oxidative stress underlying cardiovascular, neurological

and immunological disorders in response to environmental risk factors and the existing research gaps (including a definition and discussion of the usefulness of oxidative stress biomarkers in this context [17]). We also put emphasis on emerging mechanisms based on dysregulation of the circadian clock, the microbiome, epigenetic pathways and cognitive function by environmental stressors. Several articles within this Special Issue thematically cover chemical environmental stressors such as air pollution [18–20], nano/microplastic particles [21], other toxic environmental chemicals (e.g. heavy metals or pesticides as well as airborne secondary toxicants) [22–24] and the behavioral risk factor waterpipe smoking [25]. We also put emphasis on articles highlighting biochemical mechanisms that explain the adverse health effects of non-chemical environmental stressors such as UV-induced damage [20,26], traffic noise exposure [27,28] and mental stress [29,30].

1. Airborne chemical pollutants

Gangwar & Rajagopalan provide an update to what extent air pollution constituents (with emphasis on particulate matter) are taken up into the organism, triggering inflammation and oxidative stress pathways and finally leading to adverse health outcomes with respect to lung and cardiovascular diseases [18]. The authors also provide a tabular overview concerning related animal as well as human studies and conclude with a brief overview on the mitigation of air pollution and how to fill research gaps in the scientific field of air pollution. Ferrara & Valacchi present new data on additive effects of UV irradiation in combination with ozone and/or diesel engine exhaust on oxidation and inflammation pathways in human skin explants [20]. The authors established that the combination of different stressors may have additive effects on most of the investigated markers, with a central role of the aryl hydrocarbon receptor. They also provide evidence for the protective potential of antioxidant cosmeceuticals. Ziegler & Pöschl report about the increased pro-inflammatory potential of nitrated α -synuclein, heat shock protein 60 and high-mobility-group box 1 protein, which are relevant in neurodegenerative and cardiovascular diseases, by measuring the activation of the Toll-like receptor 4 in cultured human monocytes (THP-1) [19]. The authors employed nitrated proteins as a model of damage-associated molecular patterns that arise upon reaction of endogenous proteins with nitrogen oxide radicals from air pollution or peroxy nitrite generated by immune cells in response to stimulation by solid particulate matter. Hu & Palic provide an overview on nano-/microplastic particle induced health effects with mechanisms relying on oxidative stress and inflammatory pathways that interestingly show similarities to the toxic effects of air pollution particles [21]. The authors

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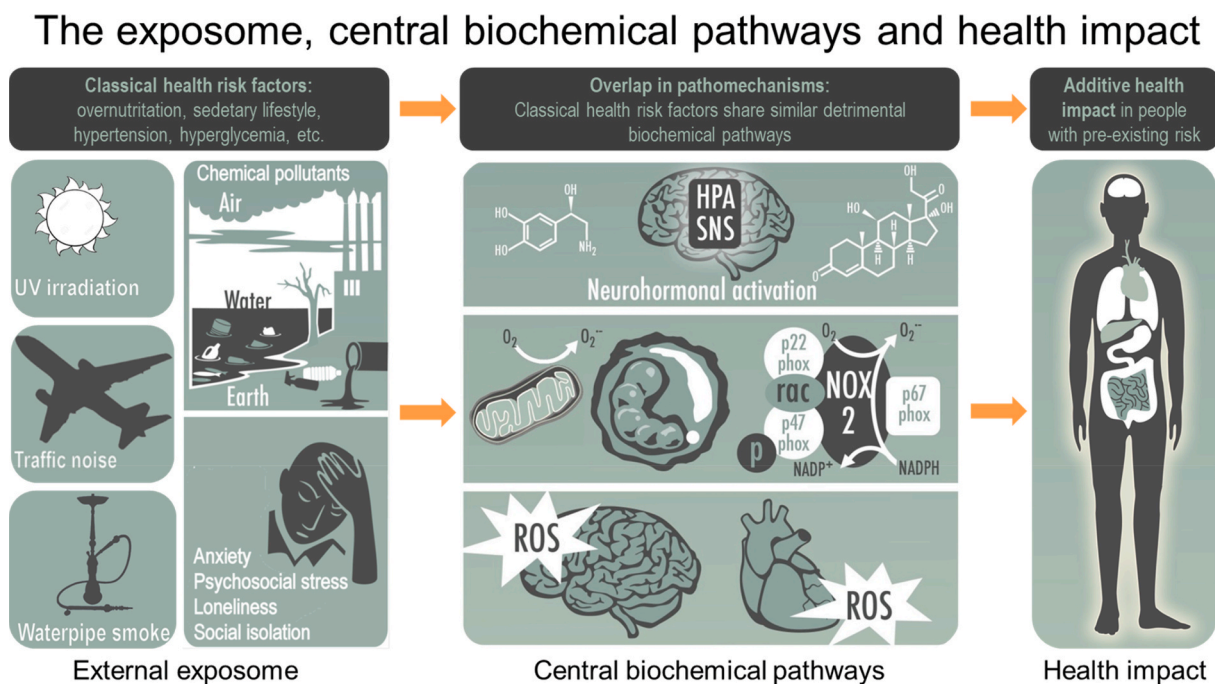


Fig. 1. Exposure to environmental risk factors (=external exposome) leads to changes of central biochemical pathways with associated health impact. The central biochemical pathways comprise stress hormone release (cortisol and catecholamines), production of reactive oxygen species by mitochondria and NADPH oxidase in activated immune cells, inflammation with tissue infiltration of activated immune cells and oxidative damage in different organs. Since classical health risk factors share similar pathomechanisms, people with existing classical health risk factors or disease (e.g. diabetes or hypertension) may experience additive adverse health effects upon exposure to environmental risk factors. HPA, hypothalamic-pituitary-adrenal axis; SNS, sympathetic nervous system; NOX-2, phagocytic NADPH oxidase (isoform 2); ROS, reactive oxygen species. Modified from [31] with permission according to the terms of the Creative Commons CC BY license. © 2019 The Authors. British Journal of Pharmacology published by John Wiley & Sons Ltd on behalf of British Pharmacological Society.

prepared their overview in the format of Adverse Outcome Pathways (AOPs) based on key events, which is also used by public health organizations and the OECD guidelines, presenting a complete tabular overview on key events, adverse health outcomes and toxicological endpoints in different organisms.

2. Other environmental chemical pollutants

Zheng & Aschner summarize the pathophysiology of heavy metals, pesticides and airborne secondary toxicants with emphasis on oxidative and electrophilic activation of the nuclear factor erythroid 2-related factor 2 (NRF2) [22]. The authors also highlight other pollutant-triggered redox and electrophilic signaling pathways (e.g. PTP1B, PTEN, HSP90 and epigenetics). Miguel & Espinosa-Diez provide an overview on the regulation of non-coding RNAs (e.g. microRNAs) by UV irradiation and a large number of environmental chemicals such as polychlorinated biphenyl (PCB), bisphenol, heavy metals, particulate matter, asbestos and pesticides [23]. The authors created tables of the health effects of different pollutants on non-coding RNA regulation, their target genes and associated health effects. Vogel & Haarmann-Stemann discuss the role of the aryl hydrocarbon receptor (AHR) for pollution mediated stress responses and inflammation with emphasis on polycyclic aromatic hydrocarbons (PAHs) and persistent organic pollutants (POPs), e.g. as contained in airborne particulate matter [24]. The authors describe in detail how AHR activation can lead to reactive oxygen species (ROS) formation and what role the interaction with other targets such as xenobiotic-responsive elements, cytochrome P450 enzymes, glutathione S-transferase, NRF2, nuclear factor- κ B and others play for pollution response. Badran & Laher summarize the adverse health effects of waterpipe (shisha) smoking via oxidative stress induction with a detailed discussion of the toxic constituents specific for waterpipe smoke and their pathobiochemical potential [25]. The authors also highlight the impact of these toxic compounds as central

players of oxidative stress leading to antioxidant and inflammatory responses in different organs and describe their association with oxidative stress markers in human and animal studies.

3. Physical and mental environmental stressors

Kremslehner & Gruber present original data on a rapid activation of glucose-6-phosphate dehydrogenase (G6PD) by acute UV irradiation, representing a novel metabolic stress adaptation process by switching to the pentose phosphate pathway (measured by MS/MS metabolomics), which was also mimicked by metformin treatment [26]. The activation of G6PD by acute UV challenges correlates with DNA damage responses (γ H2AX) and cell damage pathways in skin equivalent models of cultured primary keratinocytes and skin biopsies, but was abnormal upon chronic UV irradiation. The other work on the adverse effects of UV irradiation was already described above [20]. Steven & Münzel show new data on the additive adverse effects of aircraft noise exposure and pre-existing arterial hypertension in mice upon infusion with angiotensin-II and noise exposure for 7 days [28]. The authors demonstrate that in a hypertension model characterized by increased ROS formation (2-hydroxyethidium by HPLC), increased markers of oxidative stress (4-hydroxynonenal) and inflammation (CD68, VCAM-1, interleukins), impaired nitric oxide signaling (eNOS S-glutathionylation, plasma nitrite, pSer1177-eNOS, pVASP), endothelial dysfunction and high blood pressure that all these parameters are further aggravated by aircraft noise in the aorta, heart and brain in the presence of both risk factors. Daiber & Münzel summarize the mechanisms of adverse redox signaling and oxidative stress pathways initiated by traffic noise exposure that ultimately lead to neuronal stress responses (via the limbic system (amygdala) and the HPA axis), uncoupling and dysregulation of endothelial and neuronal nitric oxide synthase (eNOS and nNOS) as well as impaired nitric oxide signaling [27]. The authors explain how noise induces neuroinflammation, cerebral oxidative stress and release of

stress hormones, and how this neuronal activation translates to noise-induced cardiovascular dysfunction (via crosstalk of neuronal stress hormones with vasoconstrictor pathways) and damage (via activation of the phagocytic NADPH oxidase and inflammatory pathways).

Ghaemi & Michal provide an overview on the molecular mechanisms triggered by psychosocial stress with special emphasis on the role of the amygdala, a crucial structure of the fear-defense system [30]. The authors discuss different interaction nodes of mental and oxidative stress, the crosstalk with the sympathetic nervous system, preventive therapeutic interventions, and highlight recent neuroimaging data explaining the translation of increased metabolic amygdala activity to systemic inflammation and cardiometabolic diseases. Li & Xia summarize the health effects of loneliness and social isolation via stress response pathways (cortisol and catecholamines) and induction of inflammation as well as oxidative stress [29]. The authors explain how chronic psychosocial stress is strongly linked to cardiovascular diseases and highlight the central role of cerebral oxidative stress for activation of the HPA axis and the sympathetic nervous system.

4. Concluding note

Environmental stressors share common pathophysiological pathways centered on stress hormone signaling, oxidative stress and inflammation (Fig. 1) [7], which will make it almost impossible to discriminate between exposure to different environmental stressors within ongoing and future large-scale exposome studies. Oxidative stress and inflammation also represent major pathomechanisms causing cardiovascular, neurodegenerative and metabolic diseases. Accordingly, an overlap of these central pathways is indicative of additive/synergistic adverse biochemical effects in response to environmental, lifestyle and traditional health risk factors leading to aggravated pathogenesis of non-communicable diseases in a bonfire fashion [8]. Accordingly, P. Ghezzi proposes a classification of oxidative stress biomarkers (type 0–4), discusses their usefulness as direct and indirect read-outs of the in vivo footprints of environmental risk factors and whether these biomarkers may represent therapeutic targets or just represent innocent bystanders [17]. Considering the accumulation of environmental risk factors in big cities and large urbanized areas (e.g. noise, air pollution and psychosocial stress), the health problems and disease burden associated with the sum of these environmental stressors may even outperform all previous estimations. At the end, we would like to thank all the authors for their valuable contributions and we hope that they will stimulate new ideas and scientific discussion.

Declaration of competing interest

None.

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References

- [1] S.S. Lim, T. Vos, A.D. Flaxman, G. Danaei, K. Shibuya, H. Adair-Rohani, M. Amann, H.R. Anderson, K.G. Andrews, M. Aryee, C. Atkinson, L.J. Bacchus, A.N. Bahalim, K. Balakrishnan, J. Balmes, S. Barker-Collo, A. Baxter, M.L. Bell, J.D. Blore, F. Blyth, C. Bonner, G. Borges, R. Bourne, M. Boussinesq, M. Brauer, P. Brooks, N. G. Bruce, B. Brunekreef, C. Bryan-Hancock, C. Bucello, R. Buchbinder, F. Bull, R. Burnett, T.E. Byers, B. Calabria, J. Carapetis, E. Carnahan, Z. Chafe, F. Charlson, H. Chen, J.S. Chen, A.T. Cheng, J.C. Child, A. Cohen, K.E. Colson, B.C. Cowie, S. Darby, S. Darling, A. Davis, L. Degenhardt, F. Dentener, D.C. Des Jarlais, K. Devries, M. Dherani, E.L. Ding, E.R. Dorsey, T. Driscoll, K. Edmond, S.E. Ali, R. E. Engell, P.J. Erwin, S. Fahimi, G. Falder, F. Farzadfar, A. Ferrari, M.M. Finucane, S. Flaxman, F.G. Fowkes, G. Freedman, M.K. Freeman, E. Gakidou, S. Ghosh, E. Giovannucci, G. Gmel, K. Graham, R. Grainger, B. Grant, D. Gunnell, H. R. Gutierrez, W. Hall, H.W. Hoek, A. Hogan, H.D. Hosgood 3rd, D. Hoy, H. Hu, B. J. Hubbell, S.J. Hutchings, S.E. Ibeanusi, G.L. Jacklyn, R. Jasrasaria, J.B. Jonas, H. Kan, J.A. Kanis, N. Kassebaum, N. Kawakami, Y.H. Khang, S. Khatibzadeh, J. P. Khoo, C. Kok, F. Laden, R. Lalloo, Q. Lan, T. Lathlean, J.L. Leasher, J. Leigh, Y. Li, J.K. Lin, S.E. Lipshultz, S. London, R. Lozano, Y. Lu, J. Mak, R. Malekzadeh, L. Mallinger, W. Marcenes, L. March, R. Marks, R. Martin, P. McGrath, J. McGrath, S. Mehta, G.A. Mensah, T.R. Merriman, R. Micha, C. Michaud, V. Mishra, K. Mohd Hanafiah, A.A. Mokdad, L. Morawska, D. Mozaffarian, T. Murphy, M. Naghavi, B. Neal, P.K. Nelson, J.M. Nolla, R. Norman, C. Olives, S.B. Omer, J. Orchard, R. Osborne, B. Ostro, A. Page, K.D. Pandey, C.D. Parry, E. Passmore, J. Patra, N. Pearce, P.M. Pelizzari, M. Petzold, M.R. Phillips, D. Pope, C.A. Pope 3rd, J. Povles, M. Rao, H. Razavi, E.A. Rehfuess, J.T. Rehm, B. Ritz, F.P. Rivara, T. Roberts, C. Robinson, J.A. Rodriguez-Portales, I. Romieu, R. Room, L. C. Rosenfeld, A. Roy, L. Rushton, J.A. Salomon, U. Sampson, L. Sanchez-Riera, E. Sanman, A. Sapkota, S. Seedat, P. Shi, K. Shield, R. Shivakoti, G.M. Singh, D. A. Sleet, E. Smith, K.R. Smith, N.J. Stapelberg, K. Steenland, H. Stockl, L.J. Stovner, K. Straif, L. Straney, G.D. Thurston, J.H. Tran, R. Van Dingenen, A. van Donkelaar, J.L. Veerman, L. Vijayakumar, R. Weintraub, M.M. Weissman, R.A. White, H. Whiteford, S.T. Wiersma, J.D. Wilkinson, H.C. Williams, W. Williams, N. Wilson, A.D. Woolf, P. Yip, J.M. Zielinski, A.D. Lopez, C.J. Murray, M. Ezzati, M. A. Almazroo, Z.A. Memish, A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010, *Lancet* 380 (2012) 2224–2260, [https://doi.org/10.1016/S0140-6736\(12\)61766-8](https://doi.org/10.1016/S0140-6736(12)61766-8).
- [2] C.J. Murray, M. Ezzati, A.D. Flaxman, S. Lim, R. Lozano, C. Michaud, M. Naghavi, J.A. Salomon, K. Shibuya, T. Vos, D. Wikler, A.D. Lopez, GBD 2010: design, definitions, and metrics, *Lancet* 380 (2012) 2063–2066, [https://doi.org/10.1016/S0140-6736\(12\)61899-6](https://doi.org/10.1016/S0140-6736(12)61899-6).
- [3] G.A. Bray, S. Paeratakul, B.M. Popkin, Dietary fat and obesity: a review of animal, clinical and epidemiological studies, *Physiol. Behav.* 83 (2004) 549–555, <https://doi.org/10.1016/j.physbeh.2004.08.039>.
- [4] C.P. Wild, Complementing the genome with an “exposome”: the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer epidemiology, biomarkers & prevention* : a publication of the American Association for Cancer Research, cosponsored. *Am.Soc. of Prev Oncol* 14 (2005) 1847–1850, <https://doi.org/10.1158/1055-9965.EPI-05-0456>.
- [5] K. Sainani, Taking on the exposome - bringing bioinformatics tools to the environmental side of the health equation, *biomed. comput.review fall 2016* (2016) 14–21.
- [6] M. Vrijheid, The exposome: a new paradigm to study the impact of environment on health, *Thorax* 69 (2014) 876–878, <https://doi.org/10.1136/thoraxjnl-2013-204949>.
- [7] T. Münzel, A. Daiber, Environmental stressors and their impact on health and disease with focus on oxidative stress, *Antioxidants Redox Signal.* 28 (2018) 735–740, <https://doi.org/10.1089/ars.2017.7488>.
- [8] A. Daiber, J. Lelieveld, S. Steven, M. Oelze, S. Kroll-Schon, M. Sorensen, T. Münzel, The “exposome” concept - how environmental risk factors influence cardiovascular health, *Acta Biochim. Pol.* 66 (2019) 269–283, <https://doi.org/10.18388/abp.2019.2853>.
- [9] P.J. Landrigan, R. Fuller, N.J.R. Acosta, O. Adeyi, R. Arnold, N.N. Basu, A.B. Balde, R. Bertollini, S. Bose-O’Reilly, J.I. Boufford, P.N. Breyse, T. Chiles, C. Mahidol, A. M. Coll-Seck, M.L. Cropper, J. Fobil, V. Fuster, M. Greenstone, A. Haines, D. Hanrahan, D. Hunter, M. Khare, A. Krupnick, B. Lanphear, B. Lohani, K. Martin, K.V. Mathiasen, M.A. McTeer, C.J.L. Murray, J.D. Ndahimananjara, F. Perera, J. Potocnik, A.S. Preker, J. Ramesh, J. Rockstrom, C. Salinas, L.D. Samson, K. Sandilya, P.D. Sly, K.R. Smith, A. Steiner, R.B. Stewart, W.A. Suk, O.C.P. van Schayck, G.N. Yadama, K. Yumkella, M. Zhong, The Lancet Commission on pollution and health, *Lancet* 391 (2018) 462–512, [https://doi.org/10.1016/S0140-6736\(17\)32345-0](https://doi.org/10.1016/S0140-6736(17)32345-0).
- [10] Online-Link5, WHO report. Preventing disease through healthy environments. https://www.who.int/quantifying_chimpacts/publications/preventing-disease/en/, 2016. (Accessed 29 June 2020).
- [11] A.J. Cohen, M. Brauer, R. Burnett, H.R. Anderson, J. Frostad, K. Estep, K. Balakrishnan, B. Brunekreef, L. Dandona, R. Dandona, V. Feigin, G. Freedman, B. Hubbell, A. Jobling, H. Kan, L. Knibbs, Y. Liu, R. Martin, L. Morawska, C. A. Pope 3rd, H. Shin, K. Straif, G. Shaddick, M. Thomas, R. van Dingenen, A. van Donkelaar, T. Vos, C.J.L. Murray, M.H. Forouzanfar, Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015, *Lancet* 389 (2017) 1907–1918, [https://doi.org/10.1016/S0140-6736\(17\)30505-6](https://doi.org/10.1016/S0140-6736(17)30505-6).
- [12] G.B.D.R.F. Collaborators, Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, *Lancet* 390 (2017) 1345–1422, [https://doi.org/10.1016/S0140-6736\(17\)32366-8](https://doi.org/10.1016/S0140-6736(17)32366-8).
- [13] R. Burnett, H. Chen, M. Szyszkowicz, N. Fann, B. Hubbell, C.A. Pope 3rd, J.S. Apte, M. Brauer, A. Cohen, S. Weichenthal, J. Coggins, Q. Di, B. Brunekreef, J. Frostad, S. S. Lim, H. Kan, K.D. Walker, G.D. Thurston, R.B. Hayes, C.C. Lim, M.C. Turner, M. Jerrett, D. Krewski, S.M. Gapstur, W.R. Diver, B. Ostro, D. Goldberg, D.

- L. Crouse, R.V. Martin, P. Peters, L. Pinault, M. Tjepkema, A. van Donkelaar, P. J. Villeneuve, A.B. Miller, P. Yin, M. Zhou, L. Wang, N.A.H. Janssen, M. Marra, R. W. Atkinson, H. Tsang, T. Quoc Thach, J.B. Cannon, R.T. Allen, J.E. Hart, F. Laden, G. Cesaroni, F. Forastiere, G. Weinmayr, A. Jaensch, G. Nagel, H. Concin, J. V. Spadaro, Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter, *Proc. Natl. Acad. Sci. U. S. A.* 115 (2018) 9592–9597, <https://doi.org/10.1073/pnas.1803222115>.
- [14] J. Lelieveld, K. Klingmüller, A. Pozzer, U. Poschl, M. Fnais, A. Daiber, T. Münzel, Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions, *Eur. Heart J.* 40 (2019) 1590–1596, <https://doi.org/10.1093/eurheartj/ehz135>.
- [15] T. Münzel, F.P. Schmidt, S. Steven, J. Herzog, A. Daiber, M. Sorensen, Environmental noise and the cardiovascular system, *J. Am. Coll. Cardiol.* 71 (2018) 688–697, <https://doi.org/10.1016/j.jacc.2017.12.015>.
- [16] E.V. Kempen, M. Casas, G. Pershagen, M. Foraster, WHO environmental noise guidelines for the European region: a systematic review on environmental noise and cardiovascular and metabolic effects: a summary, *Int. J. Environ. Res. Publ. Health* 15 (2018) 379, <https://doi.org/10.3390/ijerph15020379>.
- [17] P. Ghezzi, Environmental risk factors and their footprints in vivo - a proposal for the classification of oxidative stress biomarkers, *Redox Biology* (2020) 101442, <https://doi.org/10.1016/j.redox.2020.101442>, in this special issue.
- [18] R.S. Gangwar, G.H. Bevan, R. Palanivel, L. Das, S. Rajagopalan, Oxidative stress pathways of air pollution mediated toxicity: recent insights, *Redox biology* (2020) 101545, <https://doi.org/10.1016/j.redox.2020.101545>, in this special issue.
- [19] K. Ziegler, A.T. Kunert, K. Reinmuth-Selzle, A.L. Leifke, D. Widera, M.G. Weller, D. Schuppan, J. Fröhlich-Nowoisky, K. Lucas, U. Pöschl, Chemical modification of pro-inflammatory proteins by peroxynitrite increases activation of TLR4 and NF-κB: implications for the health effects of air pollution and oxidative stress, *Redox Biology* (2020), <https://doi.org/10.1016/j.redox.2020.101581> in this special issue.
- [20] F. Ferrara, B. Woodby, A. Pecorelli, M.L. Schiavone, E. Pambianchi, N. Messano, J. P. Therrien, H. Choudhary, G. Valacchi, Additive effect of combined pollutants to UV induced skin OxInflammation damage. Evaluating the protective topical application of a cosmeceutical mixture formulation, *Redox biology* (2020) 101481, <https://doi.org/10.1016/j.redox.2020.101481>, in this special issue.
- [21] M. Hu, D. Palic, Micro- and nano-plastics activation of oxidative and inflammatory adverse outcome pathways, *Redox Biology* (2020), <https://doi.org/10.1016/j.redox.2020.101620> in this special issue.
- [22] F. Zheng, F.M. Goncalves, Y. Abiko, H. Li, Y. Kumagai, M. Aschner, Redox toxicology of environmental chemicals causing oxidative stress, *Redox biology* (2020) 101475, <https://doi.org/10.1016/j.redox.2020.101475>, in this special issue.
- [23] V. Miguel, S. Lamas, C. Espinosa-Diez, Role of non-coding-RNAs in response to environmental stressors and consequences on human health, *Redox Biology* (2020), <https://doi.org/10.1016/j.redox.2020.101580> in this special issue.
- [24] C.F.A. Vogel, L.S. Van Winkle, C. Esser, T. Haarmann-Stemann, The aryl hydrocarbon receptor as a target of environmental stressors - implications for pollution mediated stress and inflammatory responses, *Redox biology* (2020) 101530, <https://doi.org/10.1016/j.redox.2020.101530>, in this special issue.
- [25] M. Badran, I. Laher, Waterpipe (shisha, hookah) smoking, oxidative stress and hidden disease potential, *Redox biology* (2020) 101455, <https://doi.org/10.1016/j.redox.2020.101455>, in this special issue.
- [26] C. Kremslehner, A. Miller, R. Nica, I.-M. Nagelreiter, M.-S. Narzt, B. Golabi, V. Vorstandlechner, M. Mildner, J. Lachner, E. Tschachler, F. Ferrara, K. Klavins, M. Schosserer, J. Grillari, A. Haschemi, F. Gruber, Imaging of metabolic activity adaptations to UV stress, drugs and differentiation at cellular resolution in skin and skin equivalents – implications for oxidative UV damage, *Redox Biology* (2020), <https://doi.org/10.1016/j.redox.2020.101583> in this special issue.
- [27] A. Daiber, S. Kroller-Schon, M. Oelze, O. Hahad, H. Li, R. Schulz, S. Steven, T. Münzel, Oxidative stress and inflammation contribute to traffic noise-induced vascular and cerebral dysfunction via uncoupling of nitric oxide synthases, *Redox biology* (2020) 101506, <https://doi.org/10.1016/j.redox.2020.101506>, in this special issue.
- [28] S. Steven, K. Frenis, S. Kalinovic, M. Kvandova, M. Oelze, J. Helmstadter, O. Hahad, K. Filippou, K. Kus, C. Trevisan, K.D. Schluter, K. Boengler, S. Chlopicki, K. Frauenknecht, R. Schulz, M. Sorensen, A. Daiber, S. Kroller-Schon, T. Münzel, Exacerbation of adverse cardiovascular effects of aircraft noise in an animal model of arterial hypertension, *Redox Biology* (2020) 101515, <https://doi.org/10.1016/j.redox.2020.101515>, in this special issue.
- [29] H. Li, N. Xia, The role of oxidative stress in cardiovascular disease caused by social isolation and loneliness, *Redox Biology* (2020), <https://doi.org/10.1016/j.redox.2020.101585> in this special issue.
- [30] J. Ghaemi Keraohadi, M. Michal, The fear-defense system, emotions, and oxidative stress, *Redox Biology* (2020), <https://doi.org/10.1016/j.redox.2020.101588> in this special issue.
- [31] H. Li, A.B. Kilgallen, T. Münzel, E. Wolf, S. Lecour, R. Schulz, A. Daiber, L.W. Van Laake, Influence of mental stress and environmental toxins on circadian clocks: implications for redox regulation of the heart and cardioprotection, *Br. J. Pharmacol.* (2019), <https://doi.org/10.1111/bph.14949>.

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