Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Male C57BL/6 mice were fed with 45% kcal high-fat diet for effect of PNS was abolished by compound C (AMPK inhibitor). Concentration-dependent manner. Importantly, the protective diabetics.

or healthcare supplement for improving vascular function in ER stress and oxidative stress. These results strengthen the significantly improved endothelial function in diabetic mice through activation of AMPK/eNOS pathway and alleviation of changes were reversed by co-incubation of PNS in

endothelium-dependent relaxations in mouse aortas, (2) decreased the phosphorylation of AMPK and eNOS in both aortas and HUVECs, (3) upregulated the expression of endoplasmic reticulum (ER) stress markers such as phosphorylation of eIF2α at Ser52 and cleaved ATF6, and (4) increased the level of reactive oxygen species. These changes were reversed by co-incubation of PNS in concentration-dependent manner. Importantly, the protective effect of PNS was abolished by compound C (AMPK inhibitor).

Male C57BL/6 mice were fed with 45% kcal high-fat diet for three months to build the diabetic obese mouse model and the PNS was administered by oral gavage at 20 mg/kg body weight daily for another 4 weeks. Chronic treatment of PNS significantly improved endothelial function in diabetic mice or healthcare supplement for improving vascular function in diabetics.

doi: 10.1016/j.freeradbiomed.2021.12.088

72

Oxidative Inactivation of Cathepsin B Is Associated with Dysregulated Airway Stem Cell Proteostasis and Repair

Elizabeth Corteselli, Yvonne Janssen-Heininger, Joseph Druso, Reem Aboushousha, Maximilian MacPherson

University of Vermont, USA

Idiopathic pulmonary fibrosis (IPF) is a progressive disease characterized by repeated cycles of injury leading to aberrant airway epithelial cell repair. Specifically, dysfunctional protein processing, increased transforming growth factor beta (TGFβ) signaling, and aberrant stem cell differentiation have been observed in IPF and implicated in its pathogenesis. Although redox processes are known to play a role in IPF, the exact mechanisms by which they contribute to the progression of IPF are not well described. We previously demonstrated that the redox modification protein glutathionylation (PSSG) is increased in patients with IPF, and that the activity of the enzyme responsible for removal of this modification, glutaredoxin (GLRX), is decreased. However, the specific pathways that are affected by decreases in GLRX and resulting increased PSSG remain to be described. Herein, we investigated how PSSG of cysteine cathepsins, proteases that play a key role in degradation of protein cargo in autophagy, alters airway stem cell proteostasis. We found that PSSG of cathepsin B (CTSB) is increased in mouse airway stem cells in the absence of GLRX and in response to the pro-fibrotic stimulus TGFβ. While the expression of CTSB is increased in airway basal cells lacking GLRX, paradoxically the activity of CTSB displays a trend to decrease. Additionally, airway basal cells without GLRX have increased protein aggregation, lysosomal dysfunction, and altered autophagy. We further observed that TGFβ signaling and stem cell differentiation are markedly altered in the absence of GLRX. In a 3D organoid culture model, stem cells lacking GLRX were unable to fully differentiate to luminal cells. These findings indicate that glutathionylation of CTSB is associated with altered proteostasis in airway stem cells, which may play a role in the progression of IPF. These results contribute to a mechanistic rationale for the use of GLRX as a therapeutic in settings of fibrosis.

doi: 10.1016/j.freeradbiomed.2021.12.089

73

Children and Adolescents with COVID-19: Reduced, Oxidized Glutathione and their Ratio Level

Marina Darenkaya, Lyubov V. Rychkova, Natalya V. Semenova, Alla Petrova, Sergey I. Kolesnikov, Ekaterina Kudeyarova, Anastasia Brichagina, Lyubov Kolesnikova

Scientific Centre for Family Health and Human Reproduction Problems, Russia

Many investigations proved, that children and adolescents are less susceptible to COVID-19 than adults. They are 1% to 5% of patients with diagnosed cases of the disease. However, any age children should be in the focus of special attention, since they play a huge role in the spread of the disease. Reduced glutathione is a key intracellular antioxidant; it is involved in biochemical transformations of vitamins and other compounds, thiol-disulfide equilibrium regulation and nucleic acid synthesis, eicosanoid metabolism, etc. But currently, glutathione system changes in the pediatric population with COVID-19 are not properly investigated. The aim is to assess reduced (GSH), oxidized (GSSG) glutathione and their ratio (GSH / GSSG) level in children and adolescents with COVID-19 infection. 25 children and adolescents (average age: 14.78 ± 4.93 years) with COVID-19 were examined. According to the “case-control” principle, same age (mean age: 14.35 ± 4.02 years) practically healthy children and adolescents used as a control group. Fluorometric research methods were used. In the 7-11-year-old group with COVID-19, there was a pronounced GSH deficiency (in 86% of cases), higher GSSG values (in 57% of cases) and lower GSH/GSSG ratio values (in 100% of cases) relative to the control values. In COVID-19 12-18-years-old-group, GSH deficiency was detected in 40% of cases, higher GSSG values (in 40% of cases) and lower GSH/GSSG ratio values (in 60% of cases). The older age group (19-21-years-old) differed relative to the control values by the GSH deficiency (in 88% of cases), higher GSSG values (in 25% of cases) and lower GSH/GSSG ratio values (in 25% of cases). So, COVID-19 in children is accompanied by lower values of the GSH in the 7-11-years-old children relative to the 12-18 years old group (p=0.0124). The obtained results indicate the presence of an unfavorable trend in the reduced and oxidized forms of

doi: 10.1016/j.freeradbiomed.2021.12.090