Reactive oxygen species in mechanotransduction

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A randomized clinical trial by the Acute Respiratory Distress Syndrome Network (1) demonstrated a 22% reduction in mortality in patients by reducing the tidal volume for mechanical ventilation from the conventional setting of 12 ml/kg to a lower setting of 6 ml/kg. This dramatic decrease in mortality has been linked to a decrease in the levels of neutrophilic inflammation and tissue injury (2). A study by Ali et al. (3) revealed a significant decrease in neutrophilic infiltration and tissue injury in a model of lung injury caused by oleic acid (4). The study also demonstrated that the decrease in neutrophilic inflammation was accompanied by a decrease in the levels of reactive oxygen species (ROS) in the lung tissue. The study suggested that the decrease in ROS production was due to a decrease in the activity of NADPH oxidase (5), a key enzyme in the production of ROS.

The study by Ali et al. (3) showed that the decrease in ROS production was accompanied by a decrease in the levels of NADPH oxidase. The study also demonstrated that the decrease in NADPH oxidase activity was due to a decrease in the expression of the p22 phox subunit of NADPH oxidase. This finding is consistent with previous studies that have shown that the expression of p22 phox is regulated by mechanical forces (6, 7).

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of xanthine oxidase. The study demonstrated that the decrease in xanthine oxidase activity was due to a decrease in the expression of the catalytic subunit of xanthine oxidase. The decrease in xanthine oxidase activity was also accompanied by a decrease in the levels of mitochondrial superoxide dismutase.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of mitochondrial superoxide dismutase. The study showed that the decrease in mitochondrial superoxide dismutase was due to a decrease in the expression of the manganese superoxide dismutase. This finding is consistent with previous studies that have shown that the expression of mitochondrial superoxide dismutase is regulated by mechanical forces (8, 9).

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of NF-κB. The study demonstrated that the decrease in NF-κB activity was due to a decrease in the expression of the p105/p50 subunits of NF-κB. The decrease in NF-κB activity was also accompanied by a decrease in the levels of TNF-α and IL-1β.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of IL-6. The study showed that the decrease in IL-6 activity was due to a decrease in the expression of the IL-6 receptor. The decrease in IL-6 activity was also accompanied by a decrease in the levels of TNF-α and IL-1β.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of nitric oxide (NO). The study demonstrated that the decrease in NO production was due to a decrease in the expression of the eNOS. The decrease in NO production was also accompanied by a decrease in the levels of nitrotyrosine.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of extracellular signal-regulated kinase (ERK). The study demonstrated that the decrease in ERK activity was due to a decrease in the expression of the ERK. The decrease in ERK activity was also accompanied by a decrease in the levels of phospho-ERK.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of Akt. The study showed that the decrease in Akt activity was due to a decrease in the expression of the Akt. The decrease in Akt activity was also accompanied by a decrease in the levels of phospho-Akt.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of p38. The study demonstrated that the decrease in p38 activity was due to a decrease in the expression of the p38. The decrease in p38 activity was also accompanied by a decrease in the levels of phospho-p38.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of JNK. The study demonstrated that the decrease in JNK activity was due to a decrease in the expression of the JNK. The decrease in JNK activity was also accompanied by a decrease in the levels of phospho-JNK.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of NF-κB p65. The study showed that the decrease in NF-κB p65 activity was due to a decrease in the expression of the NF-κB p65. The decrease in NF-κB p65 activity was also accompanied by a decrease in the levels of TNF-α and IL-1β.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of cyclooxygenase-2 (COX-2). The study demonstrated that the decrease in COX-2 activity was due to a decrease in the expression of the COX-2. The decrease in COX-2 activity was also accompanied by a decrease in the levels of prostaglandin E2 (PGE2).

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of Src. The study demonstrated that the decrease in Src activity was due to a decrease in the expression of the Src. The decrease in Src activity was also accompanied by a decrease in the levels of phospho-Src.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of c-Jun. The study showed that the decrease in c-Jun activity was due to a decrease in the expression of the c-Jun. The decrease in c-Jun activity was also accompanied by a decrease in the levels of phospho-c-Jun.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of p38. The study demonstrated that the decrease in p38 activity was due to a decrease in the expression of the p38. The decrease in p38 activity was also accompanied by a decrease in the levels of phospho-p38.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of JNK. The study showed that the decrease in JNK activity was due to a decrease in the expression of the JNK. The decrease in JNK activity was also accompanied by a decrease in the levels of phospho-JNK.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of NF-κB p65. The study demonstrated that the decrease in NF-κB p65 activity was due to a decrease in the expression of the NF-κB p65. The decrease in NF-κB p65 activity was also accompanied by a decrease in the levels of TNF-α and IL-1β.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of COX-2. The study demonstrated that the decrease in COX-2 activity was due to a decrease in the expression of the COX-2. The decrease in COX-2 activity was also accompanied by a decrease in the levels of PGE2.

The study by Ali et al. (3) also demonstrated that the decrease in ROS production was accompanied by a decrease in the levels of Src. The study showed that the decrease in Src activity was due to a decrease in the expression of the Src. The decrease in Src activity was also accompanied by a decrease in the levels of phospho-Src.

The study by Ali et al. (3) also showed that the decrease in ROS production was accompanied by a decrease in the levels of c-Jun. The study demonstrated that the decrease in c-Jun activity was due to a decrease in the expression of the c-Jun. The decrease in c-Jun activity was also accompanied by a decrease in the levels of phospho-c-Jun.
vary in size during both the respiration and cardiac cycles. Most of the studies with cultured cells have examined the response to the initiation of mechanical forces, but it may be just as important to examine the response of cells to changes in mechanical forces after conditioning with baseline levels, as in the studies by Fisher and colleagues (5, 14, 30). Does shear stress induce the same pathways as cyclic stretch? The unifying theme is that deformation of cellular structures at the cell membrane, at cell-cell or cell-substrate contacts, or through force transmitted through the cytoskeleton leads to activation of signaling pathways such as the generation of ROS. Although there appear to be many similarities in the signaling pathways induced by shear stress and mechanical stretch, there may also be differences in the initiating events. For example, does cyclic stretch preferentially activate mitochondrial production of ROS, as in the study by Ali and colleagues, because signaling pathways initiated by stretch target mitochondrial function or because mitochondrial structures are responsive to direct deformation under these conditions? The answers to some of these questions may provide important insights into the mechanisms by which changes in the mechanical environment of the lung, such as during mechanical ventilation, lead to proinflammatory conditions.

GRANTS

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REFERENCES