The Role of Apoptosis Signal-Regulating Kinase 1 in Hyperoxia-Induced Lung Injury

Dhar, Saisha (School: Paul Laurence Dunbar High School)

Acute Respiratory Distress Syndrome (ARDS) is a dangerous lung disease that reduces oxygen to the essential organs of the body. The treatment that patients with ARDS receive is a combination of hyperoxia (supplemental oxygen) and mechanical ventilation, but this can inadvertently increase lung injury and mortality, warranting a need to study the mechanisms that underlie this process. One protein of interest is Apoptosis Signal-Regulating Kinase 1 (ASK1), which can be activated by stressors and plays a significant role in the inflammatory responses and cell death. The ASK1 pathway which includes the proteins Egr-1 and survivin is unclear. Survivin is a protein that inhibits apoptosis, which leads to accelerated lung injury. To study the role of ASK1 in hyperoxia-induced lung injury, A549 human lung epithelial cells were plated on a 6-well plate, with 3 wells given ASK1 inhibitor (NQDI1). This was replicated, with one plate being placed in normoxia (21% oxygen) and one in hyperoxia (90% oxygen). A western blot was performed to compare the amount of expression of Egr-1 and survivin. Change in Egr-1 expression was not significant between normoxia and hyperoxia, but survivin significantly decreased in hyperoxia. ASK1 inhibition did not affect either of the proteins. This allows survivin, essential for cell survival, to be a direct target for reducing lung injury in clinical implementation since hyperoxia reduces survivin independent of the ASK1 protein. To provide novel therapeutic options, additional studies will examine the role of ASK1 during cell stretch, which mimics mechanical ventilation, and then both hyperoxia and stretch, which more accurately models the treatment patients with ARDS receive.

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