OBJECTIVE: The objective of this study was to explore the protective effect of NAC on hyperoxia-induced lung injury and change of p38 mitogen-activated protein kinase (MAPK) expression caused by NAC treatment.
METHODS: Forty Wistar rats were randomly assigned to room air (A), hyperoxia injury (B), hyperoxia + NAC (C), hyperoxia + SB203580 (D), or hyperoxia + NAC + SB203580 (E). The lung wet/dry ratio, pathology, and location and quantity of p38 protein were detected.
RESULTS: Although pathologic changes in group B included severe alveolar edema with inflammatory cell aggregation and red blood cell leakage, the lung micrographic pictures in groups C, D, and E were improved significantly compared with group B; p38-positive cells increased in group B compared with that in group A and labeled in many types cells in lung tissue, especially in infiltrative inflammatory cells. In groups C, D, and E, the positive cells remarkably decreased compared with those in group B; the quantity of p38 MAPK was higher in group B than in group A, and p38 expression in groups C, D, and E decreased significantly compared with group B but was higher than that in the control group. There was no significant difference of p38 quantity among the 3 groups.
CONCLUSIONS: Reactive oxygen species activated phospho-p38 MAPK signaling pathway, and NAC and SB203580 treatments reduced the extent of hyperoxia-induced lung injury, as evidenced by reduction of the wet/dry ratio and lung pathology. NAC may exert a protective effect on hyperoxia-induced lung injury through attenuation of reactive oxygen species–induced p38 MAPK activation.

STUDY OF PULMONARY SURFACTANT AND SURFACTANT PROTEIN IN RATS WITH LIPOPOLYSACCHARIDE-INDUCED ACUTE LUNG INJURY

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INTRODUCTION: The abnormal metabolism of pulmonary surfactant (PS) may have some relationship to acute lung injury (ALI).
OBJECTIVE: The objective of this study was to examine the alteration trend of PS and surfactant-associated protein (SP) in rats with lipopolysaccharide (LPS)-induced ALI.
METHODS: Fifty-six adult Wistar rats were randomly divided into the normal saline (NS) group and the ALI group. The levels of mRNA of surfactant protein A (SP-A) and SP-B were measured by reverse-transcription polymerase chain reaction during intravenous LPS administration at 1, 3, 5, and 7 hours. The content and component of PS in the bronchoalveolar lavage fluid (BALF) were measured by high-performance liquid chromatography. In addition, lung dry/wet weight ratio, the protein content of BALF, alveolar oxygen partial pressure, and histologic changes were detected.
RESULTS: Compared with the NS group, the ALI group developed severe lung damage; edema, hemorrhage, and inflammation were found. Total phospholipids in BALF at 1, 3, 5, and 7 hours were lower than those in the NS group; phosphatidylcholine at 3, 5, and 7 hours was lower than that in the NS group, whereas lysophosphatidylcholine at 1, 3, 5, and 7 hours was higher than that in the NS group. The expression of SP-A and SP-B mRNA at 3, 5, and 7 hours was less than that in the NS group.
CONCLUSIONS: The changed metabolism of PS may be responsible for the pathogenesis of ALI. It is mainly demonstrated by the decrease in total phospholipids and phosphatidylcholine and the decreased expression of SP-A and SP-B mRNA. Decrease in content and change in components of PS may play an important role in severe hypoxemia in ALI.

EXPRESSION CHANGE OF AQUAPORIN 1 IN HYPEROXIC LUNG INJURY

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INTRODUCTION: Bronchopulmonary dysplasia (BPD) is a disease that is caused by prolonged high-concentration oxygen therapy, and its typical pathologic character is edema of pulmonary alveolus. Aquaporins play an important role in the fluid transition.
OBJECTIVE: The objective of this study was to examine the expression change of aquaporin 1 (AQP1) in hyperoxia-induced lung injury and the mechanism of action in lung edema.
METHODS: Thirty-two juvenile Wistar rats were randomly divided into breathing room air ($n = 8$) and hyperoxia exposure ($O_2 > 95\%$; $n = 8$ at 3, 7, and 14 days, respectively). The distribution of AQP1 in the lung tissues and its mRNA expressions were detected by immunohistochemistry and reverse-transcription polymerase chain reaction.
RESULTS: Light microscopic findings in the hyperoxia group included edema, hemorrhage, and extensive inflammatory cells. The lung wet/dry ratio, the protein content in bronchoalveolar lavage fluid, and the lung leak index in the hyperoxia group were significantly higher than those in room air group. The expression of AQP1 mRNA in the lungs was significantly decreased at

3 days of hyperoxia exposure, minimized at 7 days, and increased from 14 days. Immunohistochemistry for AQP1 was seen primarily in microvascular endothelia cells around bronchus and alveolus and interstitial cells; the positive regions were similar between the room air group and the hyperoxia group, AQP1 protein expression in the lungs was significantly decreased at 3 days of hyperoxia exposure, minimized at 7 days, but increased at 14 days. The dynamic changes of AQP1 protein level coincided with the changes of AQP1 mRNA expression.
CONCLUSIONS: Hyperoxic lung injury may induce regulative imbalance of aquaporin expression. It may be 1 of the reasons for lung edema caused by hyperoxic lung injury.

BASIC FEATURES OF HUMAN METAPNEUMOVIRUS CHINESE ISOLATE PROTEINS

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INTRODUCTION: Human metapneumovirus (hMPV), initially described in 2001, is an enveloped RNA virus of the genus *Metapneumovirus*, subfamily Pneumovirinae, family Paramyxoviridae.
OBJECTIVE: We sought to clarify the basic features of hMPV proteins.
METHODS: Rabbits were immunized with inactivated virions of hMPV Chinese isolate, CHN05-01, to yield anti-hMPV antiserum. Antiserum was used as primary antibody to detect hMPV proteins by Western blotting. NetNglyc 1.0 server, NetOglyc 3.1 server, and the NetPhos 2.0 server were applied for predicting potential glycosylation and phosphorylation sites of proteins of prototype virus of subtype A, CAN97-83.
RESULTS: The highest reactive titer of the antiserum with hMPV antigens reached 1:500 in enzyme-linked immunosorbent assay. Potential glycosylation sites of G protein and phosphorylation sites of P protein were greatest among all hMPV proteins. G protein was shown as a narrow band with molecular weight between 55 and 72 kd (~68 kd), indicating that its glycosylation level is consistent and remarkably different from that of CAN99-80 and CAN99-81. F1 subunit of fusion protein displayed molecular weight between 40 and 55 kd (~48 kd), which is consistent with previous reports.
CONCLUSIONS: Basic features of 2 major membrane proteins of Chinese hMPV isolate were clarified, which will benefit future studies on protein function and the pathogenesis of this virus.

APOPTOSIS OF ALVEOLAR TYPE II CELL AND C-JUN N-TERMINAL KINASE SIGNAL TRANSDUCTION INDUCED BY OXIDATIVE STRESS

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INTRODUCTION: Alveolar epithelial apoptosis has been described in the early stages of bronchopulmonary dysplasia. The production of reactive oxygen species during hyperoxia is thought to contribute to alveolar epithelial apoptosis, but the molecular mechanisms of oxidative stress–induced alveolar epithelial cell death is unclear.
OBJECTIVE: The objective of this study was to explore the role of the c-Jun N-terminal protein kinase (JNK) pathway in the apoptosis of alveolar epithelial cells that is induced by oxidative stress.
METHODS: Primary cultured rat alveolar type cells were treated with 500 μM hydrogen peroxide (H_2O_2) at various time intervals (0, 1, 3, 6, and 9 hours), whereas some cells were pretreated with a specific JNK inhibitor (SP600125). Mitochondrial membrane potential (MMP) change, cell survival, and apoptotic ratios were measured by fluorescence microscopy, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay, and flow cytometry analysis, respectively. The expression of phosphorylated JNK and Bax was detected by Western blot.
RESULTS: H_2O_2 treatment resulted in cell apoptosis and a decrease of MMP and cell viability in a time-dependent manner. Meanwhile, the JNK was activated and peaked at 30 minutes, and the Bax expression level was increased. Pretreated SP600125 enhanced cell viability and decreased apoptotic ratios after H_2O_2 treatment. The expression of Bax declined after using SP600125 compared with cells that were treated with H_2O_2 only.
CONCLUSIONS: High levels of oxidative stress induced cell apoptosis in a time-dependent manner. The mechanisms of oxidative stress–induced cell apoptosis involves JNK activation, Bax upregulation, and MMP decrease. JNK activation could improve the expression of Bax and play a proapoptotic role in the regulation of apoptosis that is induced by oxidative stress.

EFFECTS OF MESENCHYMAL STEM CELL TRANSPLANTATION ON CARDIAC FUNCTION, STRUCTURE, AND ELECTROPHYSIOLOGY IN RABBITS WITH DILATED CARDIOMYOPATHY

Submitted by Tian Jie

EXPRESSION CHANGE OF AQUAPORIN 1 IN HYPEROXIC LUNG INJURY

Feng Xu, Jie Hao and Liping Tan

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