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2A3 and 3F9*

Novel Lung Epithelial Antigens With Early Upregulation in Hyperoxic and Radiation Lung Injury Models

Carlos E. Girod, MD; Dong Ho Shin, MD, FCCP; Marc B. Hershenson, MD; Julian Solway, MD; Carrie A. Redlich, MD, FCCP; Laura B. Gilman, BA; and York E. Miller, MD

The alveolar epithelium responds to injury by upregulation of various specialized functions: proliferation and differentiation of epithelial cells, maintenance of electrolyte and water balance, secretion of surfactant and associated proteins, and metabolism of xenobiotics and toxins. Genes upregulated during lung epithelial injury caused by a variety of environmental agents may serve as sensitive biomarkers of mild epithelial damage thus allowing for timely intervention. We have developed two monoclonal antibodies (2A3 and 3F9) directed to freshly isolated alveolar type II (ATII) cells\(^1\) which identify alveolar epithelial antigens with highly upregulated expression in two rat models of lung epithelial injury: hyperoxia and radiation exposure. The 2A3 monoclonal antibody identifies by enzyme-linked immunosorbent assay (ELISA) and immunofluorescence freshly isolated and early-cultured ATII cells but fails to identify the antigen in lung in vivo. Since 2A3 expression occurred only during the process of isolation and culture of ATII cells, we hypothesized that ATII cell exposure to other stressful conditions, such as lung injury models, would also lead to upregulated expression of this antigen.

A rat hyperoxic lung injury model was used in which 21-day-old Sprague-Dawley rats were exposed to either normoxia or hyperoxia (≥95% FIO\(_2\)) for 8 days at sea level. Immunohistochemical studies demonstrated expression of 2A3 only in hyperoxia-exposed rats in alveolar material, macrophages, and alveolar epithelial cells. Immuno-electron microscopy confirmed that the alveolar material staining for 2A3 was tubular myelin. A second model of lung epithelial injury was studied: a rat lung radiation injury model. Six- to 8-week-old WAG/Rij Y rats were exposed to either a single radiation dose of 15 Gy to whole thorax or sham irradiation. This model provided a time course for study of the chronology of expression of 2A3.

2A3 was not detected in lungs of sham-treated rats but was identified in lungs of rats 14 days postradiation. 2A3 expression precedes the previously described inflammatory cell influx and histologic changes observed in lungs of rats 21 days postradiation. The second monoclonal antibody, 3F9, identifies an antigen polarized to the apical cell membrane of ATII and Clara cells. This antigen is specific for lung and is identified as a 172 kD cell membrane protein by Western blot analysis of both normoxic and hyperoxic rat lung preparations. This protein, p172, demonstrates dramatic (at least tenfold) upregulation in hyperoxia-exposed lungs by immunohistochemistry and Western blot analysis. The increase in p172 expression is due to more cells per alveolus expressing p172 as well as more protein expression per cell. Further study of 2A3 and 3F9 may yield new insight into ATII cell function and adaptation to injury, as well as provide sensitive biomarkers for detection of early alveolar epithelial cell damage.

**REFERENCE**


Soluble Transition Metals Mediate the Acute Pulmonary Injury and Airway Hyperreactivity Induced by Residual Oil Fly Ash Articles*

Kevin Dreher, PhD; Richard Jaskot, MS; Urmila Kodavanti, PhD; James Lehmann, MS; Darrell Winsett, BS; and Daniel Costa, ScD

Knowledge of the mechanisms responsible for the toxicity of emission source particles may provide biologically plausible explanations of the adverse health effects associated with ambient air particulate matter. This study examined the acute pulmonary toxicity of residual oil fly ash (ROFA) collected at a temperature of 250-300°C using a Teflon-coated fiberglass filter downstream from a power plant cyclone, which was burning low sulfur #6 residual oil. Sixty-day-old male Sprague-Dawley rats were instilled intratracheally (IT) with saline or an acidic ROFA suspension in saline (8.3 mg/kg). Bronchoalveolar lavage was performed on rats at 24 or 96 h post-IT and analyzed for protein, lactate dehydrogenase, albumin, and cellular content. Animals were also examined at 96 h post-IT for airway hyperreactivity (AH) using IV acetylcholine challenge. ROFA produced increases in all endpoints examined. The acidic leachate from ROFA was found to produce the same extent of injury

*From the University of Colorado Health Sciences Center, Denver (Drs. Girod and Miller and Ms. Gilman); Hanyang University School of Medicine, Seoul, Korea (Dr. Shin); University of Chicago School of Medicine (Drs. Hershenson and Solway); and Yale University School of Medicine, New Haven, Conn (Dr. Redlich).

*From the US Environmental Protection Agency, Health Effects Research Laboratory, Pulmonary Toxicology Branch, Research Triangle Park, North Carolina.

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