Particulate-induced Pulmonary Injury

Jeffrey I. Everitt. *CIIT Centers for Health Research.*

Airborne particles are of widespread environmental and occupational health concern and are known to induce a variety of important lung diseases. Health effects of inhaled particulate matter (PM) are an important priority issue of the U. S. EPA and were identified as one of the important American Chemistry Council research issues by the State of the Science effort. The CIIT particle toxicology program is focused on mechanisms of particle-induced airway injury and on understanding differences in animal model responses to inhaled PM, especially those in the ultrafine size range (< 0.1 mm diameter). The primary emphasis of work to date has been to develop a virus model of lung compromise with respiratory syncytial virus (RSV) to examine the effects of inhaled particles in individuals predisposed to pulmonary dysfunction. RSV infections are an extremely important childhood disease that predisposes individuals to the effects of inhaled toxicants. In addition to efforts in compromised animals using RSV, the CIIT particle toxicology studies have focused on developing expertise with selected endpoints that can be used to study the effects of particles on airway epithelium. These include noninvasive physiological measurements such as the determination of airway hyperresponsiveness, as well as cellular and molecular analysis of gene expression changes in lung cells following inhalation exposure to characterized aerosols.

Start and end date: January 1999 – December 2003.

Presentation(s):

Floyd, H. S., Tichelaar, J. W., Dance, S. T., Everitt, J., Whitsett, J. A., and Miller, M. S. (2003). Expression of mutant human K1-ras induces lung tumors in bitransgenic mice. *Toxicol. Sci.* 72 (1), 85. Supplement–*The Toxicologist.* (Abstract 413).

Asgharian, B., Wong, B. A., Bermudez, E., and Everitt, J. I. (2000). A model of clearance of titanium dioxide from the rat lung. *Toxicol. Sci.* 60(1), 195. Supplement–*The Toxicologist* (Abstract 928).

Bermudez, E., Mangum, J. B., Reverdy, E. E., Wong, B. A., Asgharian, B., Hext, P. M., Warheit, D. B, and Everitt, J. I. (2000). Pulmonary responses of rats, mice, and hamsters to inhaled titanium dioxide (TiO_2). *Toxicol. Sci*. 54(1), 314–315. Supplement–*The Toxicologist* (Abstract 1476).

Bermudez, E., Mangum, J. B., Wong, B. A., Asgharian, B., Hext, P. M., Warheit, D. B., and Everitt, J. I. (2000). Pulmonary responses of rats, mice, and hamsters to inhaled ultrafine titanium dioxide ($UTiO_2$). *Toxicol. Sci.* 60(1), 195. Supplement–*The Toxicologist* (Abstract 929).

DeLorme, M. P., Reverdy, E. E., Everitt, J. I., Mangum, J., and Moss, O. R. (2000). Characterization of pulmonary inflammation following intranasal instillation of endotoxin in BALB/c mice. Presentation at the Lovelace Respiratory Research Institute International Symposium: Susceptibility Factors for Respiratory Diseases, Santa Fe, NM, October.

DeLorme, M. P., Reverdy, E. E., Everitt, J. I., and Moss, O. R. (2000). Development of a compromised animal model of pulmonary inflammation. Presented at the North Carolina Chapter of the Society of Toxicology Spring Meeting, Research Triangle Park, NC.

DeLorme, M. P., Reverdy, E. E., Everitt, J. I., and Moss, O. R. (2000). Effect of titanium dioxide exposure to BALB/c mice with endotoxin-induced pulmonary inflammation. *Toxicol. Sci.* 60(1), 195. Supplement–*The Toxicologist* (Abstract 926).

DeLorme, M. P., and Moss, O. R. (2002). Interstrain differences in airway responsiveness to methacholine challenge observed in unrestrained, but not in restrained, plethysmography of mice. *Toxicol. Sci*. 66 (1), 98–99. Supplement–*The Toxicologist*. (Abstract 481).

Everitt, J. I. (2002). Use of laser capture microdissection (LCM) in molecular toxicology research. *Toxicol. Sci*. 66 (1), 1. Supplement–*The Toxicologist*. (Abstract 1).

Moss, O. R., Bermudez, E., and Everitt, J. E. (2003). Toxicogenomic approaches to particle-induced lung disease. Poster presentation at first annual science meeting of the Long–Range Research Initiative, American Chemistry Council, Herndon, VA, June 24–25.

Reverdy, E. E., Bermudez, E., Mangum, J. B., Asgharian, B., and Everitt, J. I. (2000). The relationship of protein carbonyl levels to inflammatory responses in bronchoalveolar lavage fluid in rats, mice, and hamsters following inhaled pigmentary titanium dioxide. *Toxicol. Sci.* 54(1), 13. Supplement–*The Toxicologist* (Abstract 64).

Wolf, D. C., Hardisty, J. F., Miller, R. T., and Everitt, J. I. (2002). Integrating toxicologic pathology into compound evaluation and risk assessment. *Toxicol. Sci*. 66 (1), 1. Supplement–*The Toxicologist*. (Abstract 4).

Peer-reviewed publication(s):

Mangum, J. B., Bermudez, E., Sar, M., and Everitt, J. I. (2004). Osteopontin expression in particle-induced lung disease. *Exp. Lung. Res.* 30, 585–598.

Hill, G. D., Mangum, J. B., Moss, O. R., and Everitt, J. I. (2003). Soluble ICAM-1, MCP-1, and MIP-2 protein secretion by rat pleural mesothelial cells following exposure to amosite asbestos. *Exp. Lung Res.* 29, 277–290.

Hext, P. M., Warheit, D. B., Mangum, J., Asgharian, B., Wong, B., Bermudez, E., and Everitt, J. (2002). Comparison of the pulmonary responses to inhaled pigmentary and ultrafine titanium dioxide particles in the rat, mouse, and hamster. *Ann. Occup. Hyg.* 46, 191–196.

Dye, J. A., McGee, J. K., Winsett, D. W., Ledbetter, A. D., Everitt, J. I., Ghio, A. J., and Costa, D. L. (2001). Acute pulmonary toxicity of particulate matter (PM) filter extracts in rats: Coherence with hospital admissions of Utah Valley residents. *Environ. Health Perspect.* 109(supplement 3), 395–403.

Calderón-Garcidueñas, L., Devlin, R. B., and Miller, F. J. (2000). Respiratory tract pathology and cytokine imbalance in clinically healthy children chronically and sequentially exposed to air pollutants. *Med. Hypotheses* 55(5), 373–378.

Everitt, J. I., Mangum, J. B., Bermudez, E., Wong, B. A., Asgharian, B., Reverdy, E. E., Hext, P. M., and Warheit, D. B. (2000). Comparison of selected pulmonary responses of rats, mice, and Syrian golden hamsters to inhaled pigmentary titanium dioxide. *Inhal. Toxicol.* 12(supplement 3), 275–282.

Reverdy, E. E., Bermudez, E., Mangum, J. B., Asgharian, B., Wong, B., and Everitt, J. I. (2000). Protein carbonyls in bronchoalveolar lavage fluid in mice, rats, and hamsters following inhalation of pigmentary titanium dioxide particles. *Inhal. Toxicol.* 12(supplement 3), 283–289.

Other publication(s):

Everitt, J. I. and Gross, E. A. (2005). Chapter 21: Euthanasia and Necropsy. In *The Laboratory Rat*, Second edition (M. A. Suckow, S. H. Weisbroth, and C. L. Franklin, editors), pp. 665–678, Elsevier, St. Louis, MO.

Vincent, R., Kumarathasan, P., Goegan, P., Bjamason, S. G., Guénette, J., Bérubé, D., Adamson, I. Y., Desjardins, S., Burnett, R. T., and Miller, F. J. (2001). Inhalation toxicology of ambient particulate matter: Acute cardiovascular effects of urban particles in Wistar rats. *Health Effects Institute Research Report* No. 104, Health Effects Institute, Boston, MA.

Sponsors in addition to the LRI: None.

Abstract revision date: January 2006.