Immunological Effect of $PM_{2.5}$ on Cytokine Production in Female Wistar Rats[1]

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Objective To investigate the immunological effect of $PM_{2.5}$ on cytokine production in female Wistar rats. **Methods** Female Wistar rats were given 0.3 mg, 0.75 mg, 2 mg, 5 mg of $PM_{2.5}$ per 0.5 mL saline, respectively. Saline was used as the negative control. TNF-α and IL-6 levels in the branchoalveolar lavage were measured by ELISA, and mRNA expression levels in lung tissue were detected by RT-PCR. Alveolar macrophages were collected for testing phogacytic function. **Results** Exposure to $PM_{2.5}$ stimulated TNF-α production in a dose-dependent manner ($P<0.05$), However, no statistically significant difference was found. No time-dependent change in TNF-α and IL-6 production was found. TNF-α and IL-6 mRNA expressions were induced by $PM_{2.5}$-exposure. The phagocytic rate (PR) was significantly decreased by $PM_{2.5}$ treatment. **Conclusion** $PM_{2.5}$ exposure increases inflammation response of the lung in a dose-dependent manner. Moreover, tissue injury induced by $PM_{2.5}$ may be related to altered production of cytokines. $PM_{2.5}$ may impair the phagocytic activity of alveolar macrophages.

Key words: $PM_{2.5}$; Inflammation; Cytokine; Phagocytic function

REFERENCES

1. Pope C A, Burnett R T, Thun M J, *et al.* (2002). Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *J Am Med Assoc* **287**, 1132-1141.
2. Schwartz J (2000). Harvesting and long term exposure effects in the relation between air pollution and mortality. *Am J Epidemiol* **151**, 440-448.
3. Wall S M, John W, Ondo J L (1988). Measurement of aerosol size distributions for nitrate and major ionic species. *Atmos Environ* **22**, 1649-1656.
4. Driscoll K E, Howard B W, Carter J M, *et al.* (1996). Chemokine expression by rat lung epithelial cells: effects of *in vitro* and *in vivo* mineral dust exposure. *Am J Pathol* **149**, 627-637.
5. Becker S, Soukup J M, Gilmour M I (1996). Stimulation of human and rat alveolar macrophages by urban air particulates: effects on oxidant radical generation and cytokine production. *Toxicol Appl Pharmacol* **141**, 637-648.
6. Driscoll K E, Carter J M, Hassenbein D G, *et al.* (1997). Cytokines and particle-induced inflammatory cell recruitment. *Environ Health Perspect* **105**(Suppl 5), 1159-1164.
7. Finkelstein J N, Johnston C, Barrett T, *et al.* (1997). Particulate-cell interactions and pulmonary cytokine expression. *Environ Health Perspect* **105**(Suppl 5), 1179-1182.
8. Brain J D (1992). Mechanisms, measurement, and significance of lung macrophage function. *Environ Health Perspect* **97**, 5-10.
9. Ghio A J, Richards J H, Carter J D, *et al*. (2000). Accumulation of iron in the rate lung after tracheal instillation of diesel particles. *Toxicol Pathol* **28**, 619-627.
10. Murphy S A, BéruBé K A, Pooley F D, *et al*. (1998). The response of lung epithelium to well characterised fine particles. *Life Sci* **62**, 1789-1799.
11. Kodavanti U P, Jaskot R H, Su W Y, *et al*. (1997). Genetic variability in combustion particle-induced chronic lung injury. *Am J Physiol* **272**, L521-L532.
12. Robert V H (1999). Theory and Practice of Cytokine Assessment in Immunotoxicology. *Methods* **19**, 17-27.
13. Driscoll K E (1994). Macrophage inflammatory proteins: biology and role in pulmonary inflammation. *Exp Lung Res* **20**, 473-489.
14. Driscoll K E (2000). TNF-α and MIP-2: role in particle-induced inflammation and regulation by oxidative stress. *Toxicology Letters* **112-113**, 177-184.
15. Florence T, Beatriz G F, Lester K (2003). Reactive oxygen species in pulmonary inflammation by ambient particulates. *Free Radical Biology & Medicine* **35**, 327-340.
16. Shukla A, Timblin C, BeruBe K, *et al*. (2000). Inhaled particulate matter causes expression of nuclear factor (NF)-kappaB-related genes and oxidant-dependent NF-kappa B activation in vitro. *Am J Respir Cell Mol Biol* **23**, 182-187.
17. Dong W, Lewtas J, Luster M I (1996). Role of endotoxin in tumor necrosis factor expression from alveolar macrophages treated with urban air particles. *Exp Lung Res* **22**, 577-592.

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18. Becker S, Soukup J M, Gilmour M I, *et al*. (1996). Stimulation of human and rat alveolar macrophages by urban air particulates: effects on oxidant radical generation and cytokine production. *Toxicol Appl Pharmaco* **141**, 637-648.
19. Lundborg M, Johard U, Stbom L L, *et al*. (2001). Human alveolar macrophage phagocytic function is impaired by aggregates of ultrafine carbon particles. *Environmental Research Section A* **86**, 244-253.
20. Creutzenberg O, Bellmann B, Muhle H, *et al*. (1998). Lung clearance and retention of toner, TiO2, and crystalline silica, utilizing a tracer technique during chronic inhalation exposure in Syrian Golden hamsters. *Inhalation Toxicol* **10**, 731-751.
21. Moller W, Hofer T, Ziesenis A, *et al*. (2002). Ultrafine Particles Cause Cytoskeletal Dysfunctions in Macrophages. *Toxicol Appl Pharmacol* **182**, 197-207.
22. Henderson R , Pickrell J A, Jones R K, *et al*. (1988). Response of rodents to inhaled diluted diesel exhaust: biochemical and cytological changes in bronchoalveolar lavage fluid and in lung tissue. *Fundam Appl Toxicol* **11**, 546-567.
23. Mauderly J L, Jones R K, Griffith W C, *et al*. (1987b). Diesel exhaust is a pulmonary carcinogen in rats exposed chronically by inhalation. *Fundam Appl Toxicol* **9**, 208-221.
24. Wolff R K, Henderson R F, Snipes M B, *et al*. (1987). Alterations in particle accumulation and clearance in lungs of rats chronically exposed to diesel exhaust. *Fundam Appl Toxicol* **9**, 154-166.
25. Driscoll K E, Carter, J M, Howard, B W, *et al*. (1994). Mutagenesis in rats lung epithelial cells *in vivo* silica exposure of *ex vivo* exposure to inflammatory cells. *Am J Respir Crit Care Med* **149**, A553.

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