LETTERS TO THE EDITOR

Emphysema, lung disease and retinoic acid

To the editor — The recent article¹ by Massaro & Massaro concerning the abrogation of experimental pulmonary emphysema by retinoic acid (RA) leaves the impression that the use of this agent represents an entirely new treatment for lung disease. This is not the case. In 1979, this laboratory described the effects of RA in experimental pulmonary fibrosis². It was hypothesized that RA might arrest the alveolar epithelial proliferation occurring in this disease process and thereby reduce lung damage. While no such effect was observed during the eight months that the animals (hamsters) were fed RA, there was nevertheless a sustained increase in alveolar macrophages between the months 4–8, suggesting that RA may stimulate these cells. It was speculated that RA might reduce the extent of lung injury with lower doses of the fibrosing agent (N-nitroso-N-methylurethane), but such studies were never undertaken.

We have also become concerned with the treatment of pulmonary emphysema, publishing work³ that demonstrates that intratracheal administration of hyaluronic acid ameliorates alveolar injury in the same elastase model used by the Massaros. This route of administration concentrates the hyaluronic acid in the lungs, allowing for the use of smaller doses, and may be equally effective with regard to RA. In view of the possible teratogenic effects of high doses of RA, aerosolization of this agent may be the treatment of choice.

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Massaro & Massaro reply — Dr. Cantor states that our article “leaves the impression that the use of this agent [retinoic acid] represents an entirely new treatment for lung disease.” We have carefully reread our paper with that possibility in mind but have been unable to find anything (words or nuances) that should have led him to that conclusion. We are aware of studies in humans where retinol, a precursor of retinoic acid, has been used in the treatment of lung disease^{4–6} but our work specifically addresses the use of retinoic acid to induce the formation of alveoli in an animal model of

human emphysema. We would be eager to learn about any earlier work, published or unpublished, on the use of retinoids for this purpose.

The hypothesis that retinoic acid might arrest alveolar epithelial proliferation in experimental fibrosis² is interesting but entirely unrelated to our work on alveolar regeneration in elastase-induced emphysema. Cantor's work⁷ showing that the intratracheal administration of hyaluronic acid ameliorates alveolar injury in rats treated with elastase is also interesting but also clearly unrelated to our work. He examines prevention of the induction of emphysema by elastase, whereas we look at the abrogation of key components of already established emphysema.

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1. Massaro, G.D. & Massaro, D. Retinoic acid treatment abrogates elastase-induced pulmonary emphysema in rats. *Nature Med.* 3, 675–677 (1997).
2. Cantor, J.O., Shapiro, S.S., di Sant'Agnes, P.A., Cerreta, J.M. & Trown, P.W. Possible stimulatory effect of retinoic acid on pulmonary macrophages. *Experientia* 35, 895–896 (1979).
3. Cantor, J.O., Cerreta, J.M., Armand, G. & Turino, G.M. Further investigation of the use of intratracheally administered hyaluronic acid to ameliorate elastase-induced emphysema. *Exper. Lung Res.* 23, 229–244 (1997).
4. Paiva, S. *et al.* Assessment of vitamin A status in chronic obstructive pulmonary disease patients and healthy smokers. *Am J. Clin. Nutr.* 64, 928–934 (1996).
5. Shena, J.P., Kennedy, K.A., Chytil, F. & Stahlman, M.T. Clinical trial of vitamin A supplementation in infants susceptible to bronchopulmonary dysplasia. *J. Pediatr.* 111, 269–277 (1987).
6. Pearson, E., Bose, C. & Snidow, T. Trial of vitamin A supplementation in very low birth weight infants at risk for bronchopulmonary dysplasia. *J. Pediatr.* 121, 420–427 (1992).
7. Cantor, J.O., Cerreta, J.M., Keller, S. & Turino, G.M. Modulation of airspace enlargement in elastase-induced emphysema by intratracheal instillation of hyaluronidase and hyaluronic acid. *Exp. Lung Res.* 21, 423–436 (1995).

Erratum

Changes to the letter from Shibo Jiang (*Nature Med.* 3, 367–368; 1997), resulted in some of the references being misnumbered. The correct set of references is available from the author via e-mail (sjiang@nybc.org).

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(*Anal. Biochem.* 225:163.1995. *Biotechniques*. 19:942. 1995.)

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