Correspondence

Inhibition of Epithelial Sodium Channels and Reduction of Ciliary Function in Influenza

To the Editor:

Pittet and coworkers reported a reduction of tracheal mucociliary velocity and associated reduced clearance of pneumococci in a murine model of influenza virus infection (1). The authors reported on movement of latex beads as a measure of ciliary beating visualized by confocal microscopy, and found that 6 days after influenza virus infection there was no evidence of ciliary movement. At that time point histologic investigations showed a regenerated intact tracheal epithelium despite the ongoing presence of influenza virus. The presence of intact epithelium with a lack of ciliary beating indicates an influenza-induced reduction of function of the ciliary apparatus. Ciliary function is dependent on calcium and sodium influx through calcium and sodium channels into the respiratory epithelial cell. In cultured ovine tracheal cells the cholinergic receptor agonist–induced increase in ciliary beat frequency was abolished by the sodium channel blocker amiloride (2).

Influenza virus inhibits amiloride-sensitive sodium channels in respiratory epithelia through binding of viral hemagglutinin to a cell-surface receptor, which then activates phospholipase C and protein kinase C (3, 4). Future investigations need to clarify whether the reduced mucociliary velocity in intact respiratory epithelium in the recovery phase of influenza (Day 6 or later) is related to reduced sodium channel function reflected in reduced intracellular sodium as a marker of sodium influx. Should the role of sodium channel dysfunction in influenza-induced reduction of mucociliary velocity be confirmed, a potential pathway for correction of the observed abnormality is opened. β-agonists can activate epithelial sodium channels via β-receptor–mediated generation of cAMP through protein kinase A activation (5). β-agonists have been shown to increase ciliary beat frequency in the trachea of beagles in an *in vivo* model (6). The effectiveness of β-agonists, however, may be limited because a previous investigation noted a reduction in β-receptor function in a mouse model of influenza (7). This reduction of β-receptor function was in the murine model of respiratory syncytial virus infection found to be due to the activity of KC, the murine homolog of CXCL8, on G protein–coupled receptor kinase 2, which mediated an uncoupling of β-adrenergic receptors from adenylyl cyclase (8).

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References

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Retraction of Two Articles

From the Editor:

Following an investigation by the staff of the American Thoracic Society as well as the University of Louisville, and at the request of the authors, the *American Journal of Respiratory Cell and Molecular Biology* has agreed to retract the following articles due to concerns related to digital manipulations and image duplications that were performed by the first (also corresponding) author without the knowledge of the coauthors, bringing into question the validity of the findings: ShouWei Han, Hilda N. Rivera, and Jesse Roman (2005) "Peroxisome proliferator–activated receptor-γ ligands inhibit α5 integrin gene transcription in non–small cell lung carcinoma cells" (1); and ShouWei Han, Jeffrey D. Ritzenthaler, XiaoJuan Sun, Ying Zheng, and Jesse Roman (2009) "Activation of peroxisome proliferator–activated receptor β/δ induces lung cancer growth via peroxisome proliferator–activated receptor coactivator γ-1α" (2).

The first author has not responded to requests by coauthors. Therefore, the coauthors have requested retraction of these articles and apologize to the readers of the journal.

The Editor
the American Journal of Respiratory Cell and Molecular Biology

On Behalf of the American Thoracic Society

References

1. Han S, Rivera HN, Roman J. Peroxisome proliferator–activated receptor-γ ligands inhibit α5 integrin gene transcription in non–small cell lung carcinoma cells. *Am J Respir Cell Mol Biol* 2005;32:350–359.
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Erratum: α5β1-Integrin Expression Is Essential for Tumor Progression in Experimental Lung Cancer

There was an error in a figure published in the article by Jesse Roman, Jeffrey D. Ritzenthaler, Sussane Roser-Page, XiaoJuan Sun, and ShouWei Han (2010) "α5β1-Integrin expression is