**Mycoplasma pneumoniae Antigens Stimulate Interleukin-8** *

Kathryn Chimura, BA; Ryan D. Lutz, BS; Hirofumi Chiba, MD, PhD; Mari S. Nunata, MD, PhD; Hee-Jung Choi, MD, PhD; Giamila Fantuzzi, PhD; Dennis R. Voelker, PhD; and Edward D. Chan, MD

(Abstr) **CHEST 2003; 123:425S**

Abbreviations: IL = interleukin; MMF = mycoplasma membrane fraction

Asthma is characterized by the presence of airway inflammation that results in bronchial hyperresponsiveness and symptoms of airflow obstruction. Persistent and severe asthma may have an eosinophilic or noneosinophilic infiltration of the airways, the latter characterized by a profusion of neutrophils. More recent findings implicate that neutrophils may play a role in the irreversible airflow limitation seen in asthma. There is evidence that some chronic asthmatics have an increased incidence of polymerase chain reaction positivity for *Mycoplasma pneumoniae* and that these patients may have a clinical response to clarithromycin therapy. In an animal model of asthma in which BALB/c mice were inoculated intranasally with *M pneumoniae*, bronchial hyperresponsiveness developed. In addition, the resultant inflammation was principally neutrophilic.

Since epithelial cells are important in the recruitment of inflammatory cells into the airways, we sought to investigate whether *mycoplasma antigens could induce interleukin (IL)-8*, a potent chemokine for neutrophils. Cultured BEAS-2B human bronchial epithelial cells stimulated with mycoplasma membrane fraction (MMF) increased IL-8 production in a dose-dependent fashion (Fig 1). Stimulation of the BEAS-2B cells with 10 ng/mL of lipopolysaccharide or with MMF plus 10 μmol/L polymyxin B demonstrated that the ability of MMF to induce IL-8 was not due to contaminating lipopolysaccharide (data not shown). In addition, MMF activated nuclear factor-κB, a transcription factor known to bind to a κB cis-element on the 5′-flanking region of the IL-8 promoter. Inhibition of nuclear factor-κB activation with an IkBα-kinase inhibitor (BAY11–7082) resulted in significant inhibition of MMF-induced IL-8 protein expression. MMF also activated all three isoforms of the mitogen-activated protein kinases. Co-culture of MMF-stimulated BEAS-2B cells with inhibitors of the mitogen-activated protein kinase pathways revealed that these serine-threonine kinases modulate MMF-induced IL-8 expression in a complex fashion. In conclusion, these findings show that mycoplasma antigens are able to induce IL-8 production in human airway epithelial cells. We hypothesize that infection with these organisms may play a role in the pathogenesis of the neutrophilic response that characterizes many cases of severe asthma.

**REFERENCES**


*From the Department of Medicine (Ms. Chimura, Mr. Lutz, Drs. Chiba, and Nunata) and Program in Cell Biology (Dr. Voelker), National Jewish Medical and Research Center; and the Divisions of Pulmonary Sciences and Critical Care Medicine (Dr. Chan) and Infectious Diseases (Dr. Choi and Fantuzzi), University of Colorado Health Sciences Center, Denver, CO. Dr. Chan is supported by National Institutes of Health grant HL66112, the Parke-Davis Atorvastatin Research Award, and the University of Colorado Health Sciences Center, Denver, CO. Divisions of Pulmonary Sciences and Critical Care Medicine (Dr. Chan) and Infectious Diseases (Drs. Chiba, and Numata) and Program in Cell Biology (Dr. Fantuzzi), National Jewish Medical and Research Center; and the Annual Lung Association Career Investigator Award. Dr. Voelker is supported by National Institutes of Health grant HL45286.

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Correspondence to: Edward D. Chan, MD, K613e, Goodman Building, National Jewish Medical and Research Center, 1400 Jackson St, Denver, CO 80206; e-mail: chane@njc.org

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**Figure 1.** MMF induces IL-8 expression in BEAS-2B cells. Cultured BEAS-2B cells were stimulated with the indicated concentrations of MMF for 48 h, and the cultured supernatant were assayed for IL-8 by electrochemiluminescence.