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Pseudomonas aeruginosa elastase induces IL-8 production in the lung cells via the epidermal growth factor/extracellular signal-regulated proteins/NFÎºB pathway

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P6

Pseudomonas aeruginosa elastase induces IL-8 production in the lung cells via the epidermal growth factor/extracellular signal-regulated proteins/NFκB pathway

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Background The induction of chemokine secretion by fibroblasts is crucial for the migration of leukocytes into the parenchyma of the injured lung. Several bacterial products activate the lung's structural as well as immune cells to produce pro inflammatory cytokines and chemokines. We report that elastase from Pseudomonas aeruginosa (PE) evokes IL-8 mRNA expression and protein secretion in nonmalignant culture of human lung fibroblasts by activating the receptor for epidermal growth factor (EGFR) and downstream mitogen-activated protein kinases (MAPK) pathway.

Methods We utilized western blot analysis to detect phosphorylation of EGFR and signal transduction intermediates. Northern blot and ELISA analyses were used to determine IL-8 RNA expression and cytokine secretion.

Results We found that the enzymatically active PE enhances IL-8mRNA and protein secretion but does not increase IL-10 or TNF expression. PE induces phosphorylation of the EGFR and the extracellular signal-regulated proteins (ERK1/2) of the MAPK pathway. Pretreatment of the cells with neutralizing antibody to EGFR or the EGFR-specific tyrphostin AG1478 markedly attenuated the PE-induced ERK1/2 activation. PE-induced IL-8 expression is also abolished in the presence of the MEK inhibitor U0126,indicating the involvement of ERK1/2 in this process.

Conclusion Taken together, the results show PE could modulate lung inflammation by exploiting the EGFR/ERK/NFκB pathway and enhancing IL-8 production by lung fibroblasts.