

## **HUMAN MAST CELL TRYPTASE STIMULATES NEUTROPHIL MIGRATION THROUGH BRONCHIAL EPITHELIUM**

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Infiltration of neutrophils into the lumen of the airways is a common feature of the respiratory inflammatory process. Mast cells may play a certain role in the regulation of this neutrophil migration by release of specific products as histamine, serine proteases, and multiple cytokines. A bilayer of cultured endothelial and bronchial epithelial cells was used as a model for the blood-air barrier, in which the migration of neutrophils was studied in the presence of different stimuli. Neutrophils were obtained from normal, non-smoking volunteers and labeled with a fluorescent marker. Confluent bilayers of cultured cells, pre-treated with 10 ng/ml TNF- $\alpha$  and IL-1 $\beta$ , showed a low spontaneous migration of neutrophils ( $1.9 \pm 0.4\%$ , n=4). Pre-incubation followed by fMLP ( $10^{-6}$  M) stimulation resulted in  $45.6 \pm 5.8\%$  migration (positive control). TNF- $\alpha$  ( $10$  ng/ml) and histamine ( $10^{-5}$  and  $10^{-6}$  M) were able to induce neutrophil migration through the cellular layers ( $13.3 \pm 2.5\%$  and  $17.4 \pm 0.6\%$ , resp.). This induction was independent of pre-incubation of the bilayer. Tryptase ( $10$  mU/ml) induced neutrophil migration ( $8.6 \pm 1.2\%$ , n=4), which was significantly increased to  $21.8 \pm 0.9\%$  after pre-treatment of the bilayer with TNF- $\alpha$  and IL-1 $\beta$ . In conclusion: a number of mast cell products are able to stimulate migration of neutrophils through a bilayer of endothelial and bronchial epithelial cells.