MAST CELLS AND NEUROENDOCRINE CELLS IN HUMAN AND RAT'S LUNG (A LITERARY REVIEW)

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Abstract
The following review present scientific literature on lung mast cells and pulmonary neuroendocrine cells in Human and rat's lung Particular attention is paid to the location, morphrology and arrangement of these cells in lung. Paul Ehrlich in 1878 (1) is the first author, who describe mast cells as effectors of allergy, particularly in the early and acute phases of allergic reactions. Ehrlich's initial view of mast cells, as metachromatic, granulated cells implicated in the nutrition of the surrounding tissue has change gradually during the years.
The detailed morphology of pulmonary neuroendocrine (NE) cells has been defined only during the last decade. The purpose of this paper is to present the main morphologic features of the NE cells, to review the location, development and functional significance of these cells.
Keywords: *mast cells, endocrine cells, lung*

Introduction
Mast cells are found in lung tissue in concentrations of 1-10 x 106 cells/g (2). They are widely spread in loose and dense connective tissues (3) such as the pleura, peribronchial areas and alveolar septa adjacent to nerves and blood vessels, particularly small arterioles and venules, and in the epithelium of upper and lower respiratory tract (4). Also they could be found free in the bronchial lumen (5, 6). Increased numbers of mast cells have been identified in humans in conditions of excessive pulmonary blood flow and chronic left ventricular decompensation (7), and in association with pulmonary fibrosis (8) as well. Whereas in rats, mast cells has been noted in chronic hypoxic states proliferation (9).
Pulmonary neuroendocrine cells (PNEC) are specialized airway epithelial cells that are found as solitary cells or as clusters called neuroepithelial bodies (NEB) in the lung. They are located in the nasal respiratory epithelium, laryngeal mucosa and in the entire respiratory tract from the trachea to the terminal airways.Both PNEC and NEB exist from fetal stage and neonatal stage in lungs airway area (10).

Purpose and tasks
The main purpose of this article is to present a literary review of the morphological characteristics of mast cells and endocrine cells in human and rat lung.
To achieve this aim, we set out the following main tasks:
1. To review our available literature related to mast cell and neuroendocrine cell morphology.
2. To present contemporary articles that are related to lung mast cell and neuroendocrine cell research.
3. To establish the current state of human and rat lung-related studies of mast cell end endocrine cells.

Literary review
PNEC and NEB cells are bottle- or flask-like in shape, and reach from the basement membrane to the lumen. They can be distinguished by their profile of bioactive amines and peptides- serotonin, calcitonin, calcitonin gene-related peptide (CGRP), chromogranin A, gastrin-releasing peptide (GRP), and cholecystokinin. These cells can be a source of lung cancer- mostly, small cell carcinoma of the lung, and bronchial carcinoid tumor. More

specific cell markers are immunoreactivity to peptide hormones (bombesin, calcitonin, leu-enkephalin) identified so far in NE cells of human lung, and immunoreactivity to serotonin found in both human and animal lungs (11).

At the ultrastructural level, NE cells posses dense core granules (90-150 nm in diameter), consist of amine and peptide hormones (11).

The single NE cells are found throughout the tracheobronchial epithelium, whereas NEB are located only within the intrapulmonary airways (12).

PNEC function is connected to chemoreceptors in hypoxia detection. This is best supported by the presence of an oxygen-sensitive potassium channel coupled to an oxygen sensory protein in the lumenal membrane. They are involved in regulating localized epithelial cell growth and regeneration through a paracrine mechanism.They also contain neuroactive substances which are released from basal cytoplasm and they induce autonomic nerve terminals or vasculature in the deep lamina propria (13).

In the fetal lung, they are frequently located at the branching points of airway tubules, and in humans are present by 10 weeks gestation. Peptides and amines released by PNEC are involved in normal fetal lung development including branching morphogenesis (14).

Two main types of mast cells are recognised in humans by their protease content. One population contains only tryptase (MCT) while the second one contains tryptase, chymase, carboxypeptidase A and cathepsin G (MCTC) (15). A rare third population containing only chymase (MCC) has also been reported (16, 17) . Also a remarkably rapid conversion of MCTC cells to MCT has been found in co-culture with human airway epithelium (18).The MCT phenotype is typically located at mucosal surfaces such as the nasal and bronchial epithelium in rhinitis and asthma, and the bronchial lamina propria (19, 20). The MCTC phenotype is found in connective tissues such as normal skin, the airway smooth muscle bundles in asthma (21) and atherosclerotic lesions (22).

Andersson and colleagues (23) have performed a detailed immunohistochemical and morphological phenotypic analysis of mast cells in human lung. According to the shape, they prove more circular MCTC than MCT in all compartments except the alveoli. As in previous studies, MCT were the dominant cells in the airways and alveoli.MCTC were more common in the pleura.

The expression of the high-affinity IgE receptor and histidine decarboxylase was relatively high in airway MCT and MCTC, but absent in alveolar mast cells.Renin was highly expressed only in pulmonary vascular MCTC. Basic

FGF and VEGF were expressed in airway, alveolar and pulmonary vascular MCT,and large airway, and pulmonary vascular MCTC.It is proved that enzymatically dispersed parenchymal human lung mast cells with smaller diameter consistently release less histamine and PGD2 than large mast cells following IgE-dependent activation (24).

Two subtypes of mature mast cells are described in rodents as well: mucosal mast cells (MMCs) and connective tissue mast cells (CTMCs) (25). In mouse, MMCs reside in the mucosal epithelium of the lung and gastrointestinal tract, and their protease content is characterized by the chymases mouse Mast Cell Proteases, mMCP-1 and mMCP-2, which are bound to chondroitin sulfate chains of serglycin proteoglycans, whereas CTMCs are found in the intestinal submucosa, peritoneum, and skin and contain the chymase mMCP-4, the tryptases mMCP-5 and mMCP-6, and carboxypeptidase A (mCPA) bound to heparin chains of serglycin proteoglycans (26, 27, 28, 29). MMCs and CTMCs also differ in their ability to secret histamine and lipid mediators. Upon activation, MMCs release small amounts of histamine and large quantities of cysteinyl leukotrienes, whereas CTMCs release higher levels

of histamine and prostaglandin D (30).
It is proved that mast cell heterogeneity in peripheral tissues is much more dynamic than the two mast cell subsets traditionally described. For example both tracheal constitutive CTMCs and induced MMCs from sensitized mice analyzed by immunohistochemistry are presented with all six mast cell proteases (31).

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