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Evaluation of chitinase activity and concentration across diverse biological specimens in patients with well-characterized respiratory diseases

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Streszczenie w języku angielskim

Human chitinases belong to the glycoside hydrolase family whose primary function is the degradation of the biopolymer chitin. Historically, these enzymes have been integral to innate immunity (e.g., against chitinous exoskeletons of parasites); nowadays, their significance is recognized within the complex network of both innate and adaptive immune mechanisms. The most prominent members of this enzymatic group are chitotriosidase (CHIT1) and acidic mammalian chitinase (AMCase). Beyond catalytically active chitinases, a wide range of organisms express chitinase-like proteins (CLPs) that, despite lacking chitinolytic activity, fulfill essential regulatory functions in the modulation of cellular and tissue responses. From a clinical perspective, the most relevant member of this second group is chitinase-3-like protein-1 (CHI3L1), also known as YKL-40.

The present doctoral dissertation is based on a series of three peer-reviewed publications, comprising one review article and two original research papers. The first article "Chitinases and chitinase-like proteins in obstructive lung diseases – current concepts and potential applications." provides a comprehensive analysis of the literature up to 2020 was performed, summarizing the current understanding of the putative role of chitinases in obstructive respiratory diseases, principally asthma and chronic obstructive pulmonary disease (COPD). The review synthesizes evidence derived from in vitro studies, animal models, and human investigations, delineating the molecular and cellular mechanisms through which these mediators contribute to inflammation, tissue remodeling, and parenchymal destruction. It systematizes knowledge on potential stimuli,

chitinase-producing cell types, and signaling pathways, and discusses the consequences of both excessive chitinase activation and reduced or absent activity (e.g., due to genetic mutations). Moreover, the influence of selected modifiers such as age, sex, and steroid therapy on chitinase activity is examined, and future research directions are proposed.

The first original article entitled “The role of chitinases in chronic airway inflammation associated with tobacco smoke exposure,” reports the findings of an observational clinical study assessing the involvement of chitinases in chronic airway inflammation triggered by tobacco smoke. This study, conducted between 2018 and 2019, enrolled 43 subjects aged > 40 years: 22 patients with mild-to-moderate COPD, 12 smokers without respiratory disease, and 9 never-smokers. Clinical records (including mMRC and CAT scores, pulmonary function tests) and induced sputum were analyzed for cellular composition, selected inflammatory cytokines, matrix metalloproteinase-9, and chitinases (YKL-40, CHIT1) using quantitative ELISA, together with assessment of CHIT1 chitinolytic activity. We found that YKL-40 concentrations were significantly higher in COPD patients compared with the other groups. Logistic regression identified elevated YKL-40 in induced sputum as an independent risk factor for COPD. Positive correlations were observed between CHIT1 concentration and activity, YKL-40 levels, and pro-inflammatory mediators (IL-8, MMP-9). Cluster analysis revealed heterogeneity within the COPD cohort, distinguishing two sub-clusters; only the second cluster exhibited a pronounced inflammatory phenotype characterized by higher inflammatory cell counts, cytokine levels, and increased chitinases concentrations and activity.

The second original article, entitled “Exploring CHIT1 and YKL-40 in tuberculous pleural effusion: Insights and implications,” describes the study evaluating the concentrations, enzymatic activity, and tissue expression patterns of chitinases in pleural effusions of diverse etiologies. This retrospective study included 66 adult patients who underwent thoracentesis at the Department of Internal Medicine, Pulmonary Diseases and Allergy, Medical University of Warsaw (2020-2023). Comprehensive pleural fluid analysis encompassed biochemical, cytological, microbiological parameters and adenosine deaminase (ADA) activity. YKL-40 and CHIT1 concentrations were measured by high-sensitivity ELISA; immunohistochemistry for these proteins was performed on selected tuberculous pleural biopsies. The highest CHIT1 and YKL-40 levels were observed in tuberculous effusions, with YKL-40 positively correlating with macrophage proportion and ADA activity. A diagnostic cut-off 500 ng mL for YKL-40 yielded 78.9 % sensitivity and 85.7 %

specificity for tuberculous pleuritis. Immunohistochemistry demonstrated robust cytoplasmic YKL-40 staining in epithelial-like and multinucleated giant cells, whereas CHIT1 staining was negligible. The study concludes that the pattern of chitinase expression in pleural tissue may serve as a valuable biomarker for differential diagnosis of granulomatous diseases.