

ABSTRACT

Respiratory pathophysiology as the premise of modern pneumology: innovation, standardization and multidisciplinary approach

This habilitation thesis, entitled *“Respiratory Pathophysiology as the Foundation of Modern Pulmonology: Innovation, Standardization and a Multidisciplinary Approach”*, provides an overview of the scientific, academic, and professional activity developed during the postdoctoral period (2020–2026). The work is structured into two main sections and reflects a research trajectory centered on personalized medicine and multidisciplinary collaboration.

After completing undergraduate studies at the University of Medicine and Pharmacy of Craiova, the professional and academic path has been structured around personalized medicine and a multidisciplinary approach. Research activity was further developed during doctoral studies at the *Iuliu Hațieganu University of Medicine and Pharmacy*, concurrently with the initiation of the academic career at the *George Emil Palade University of Medicine, Pharmacy, Science, and Technology*. This direction was subsequently consolidated through training in public health within the Master’s program in Public Health and Health Promotion at Brunel University London.

The research strategy has concretised in three distinct directions:

- **Research Direction 1:** Smoking in respiratory pathophysiology: a multidisciplinary approach and prevention strategies
- **Research Direction 2:** Neoplastic pathology in the context of respiratory pathophysiology: mechanisms and multidisciplinary approach
- **Research Direction 3:** Functional respiratory assessment as a central pillar in the pathophysiology of chronic lung diseases

The habilitation thesis complies with the national and specific criteria of the University of Medicine, Pharmacy, Science and Technology „George Emil Palade” of Targu Mures. Scientific, professional and academic achievements on thematic directions are presented in detail with references to all my research activity. The ten representative articles selected for the habilitation thesis represent the special interest for the development of personalized medicine and multidisciplinary collaboration.

Research Direction 1: Smoking in Respiratory Pathophysiology: A Multidisciplinary Approach and Preventive Strategies. This research direction is structured into two sub-directions: *Smoking as a Determinant: Mechanisms and Preventive Interventions* and *Relevant Determinants; and Multidisciplinary Approaches in the Prevention of Respiratory Diseases*.

The first sub-direction continues the research launched in the doctoral thesis and focuses on the prevention of respiratory diseases through studies in the field of tabacology. These include the assessment of smoking behavior among foster care minors from Mureș and Cluj counties, using multivariate analysis to identify predictors of smoking initiation, as well as studies addressing smoking prevalence among healthcare professionals.

This line of research is further extended through the *PaVIAGen* project (Development and testing of a Virtual Patient application based on Generative Artificial Intelligence for training healthcare professionals in delivering minimal smoking cessation advice). While the study protocol has been published, additional results focusing on expert perspectives are currently under publication. The public health component was further strengthened through postgraduate training in the Master of Science

program in Public Health and Health Promotion at Brunel University London, facilitating the integration of preventive strategies into clinical and academic practice.

The second sub-direction expands the perspective beyond tobacco use, addressing additional determinants that influence respiratory pathology. Air pollution, infectious factors, and interventions such as telemedicine are approached as modifiable elements that can contribute to reducing hospitalizations and improving patients' quality of life, within a broader preventive and multidisciplinary framework.

Research Direction 2: Neoplastic Pathology in the Context of Respiratory Pathophysiology: Mechanisms and Multidisciplinary Approach. This research direction is structured into two major components: *Lung Cancer: Pathophysiological Mechanisms and Integrated Evaluation*; and *Multidisciplinary Approaches in Oncological Pathology*.

Lung cancer is addressed through a series of studies focusing on the role of inflammatory biomarkers in the management of oncological patients. The research highlights the relevance of systemic inflammation, assessed through biomarkers such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), in relation to disease severity and prognosis.

A multicenter study conducted in collaboration with the University of Medicine and Pharmacy of Craiova emphasizes the diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the evaluation and staging of lung cancer.

Paraneoplastic syndromes are also explored as complex clinical manifestations requiring a multidisciplinary diagnostic approach. The second component of this direction reflects collaborative research with specialists in pathophysiology, extending the analysis beyond lung cancer to non-pulmonary neoplastic conditions and highlighting the importance of interdisciplinary integration in oncological research.

Research Direction 3: Functional Respiratory Assessment as a Central Pillar in the Pathophysiology of Chronic Lung Diseases. This research direction represents the core of the scientific activity, focusing on the integration of respiratory pathophysiology with advanced functional assessment methods in the evaluation of chronic lung diseases. Functional respiratory tests, including spirometry, body plethysmography, diffusion capacity (DLCO), and impulse oscillometry (IOS), are approached not only as clinical tools but as essential instruments for understanding underlying pathophysiological mechanisms. This direction is structured into three sub-directions.

The first sub-direction, *Functional Respiratory Assessment in Obstructive Pathology: Functional Expression of Pathophysiological Mechanisms*, focuses on chronic obstructive diseases, analyzed from the perspective of systemic inflammation and biomarkers, with emphasis on phenotypic and endotypic heterogeneity. Chronic obstructive pulmonary disease (COPD) is addressed both in relation to national guidelines and severe exacerbations requiring intensive care management. The analysis is extended to the COPD-obstructive sleep apnea (OSA) overlap syndrome and further to central sleep apnea, highlighting the continuum of respiratory dysfunction.

Within this framework, severe asthma is approached as a complex disease model, in which the integration of immunological mechanisms and functional evaluation enables a more precise characterization of ventilatory dysfunction. The identification of clinically relevant endotypes is possible by assessing small airways with sensitive techniques such as impulse oscillometry. These findings are further correlated with the use of biological therapies targeting type 2 (T2-high) inflammation, supporting the emerging concept of clinical and biological remission.

The second sub-direction, *Small Airways Assessment and the Role of Advanced Functional Techniques*, emphasizes the importance of modern functional investigations in respiratory pathology. Techniques such as body plethysmography, diffusion capacity measurement, and impulse oscillometry provide a more detailed understanding of pulmonary function and allow the identification of subtle or early abnormalities not detectable by conventional spirometry.

The third sub-direction, *Interstitial Lung Disease: Functional Evaluation and Pathophysiological Correlations*, focuses on interstitial pulmonary pathology from the perspective of functional assessment. In these conditions, where spirometric parameters may remain within normal limits, advanced functional investigations play a crucial role in establishing an accurate diagnosis and evaluating disease severity. The integration of functional, structural, and clinical data allows for a comprehensive and physiopathologically grounded understanding of these complex diseases.

In addition to scientific publications, the research directions are supported by research projects (as principal investigator or team member), national and international conference presentations, participation in specialized courses, invited lectures, and active involvement of students in research activities. The habilitation thesis includes a total of 127 bibliographic references supporting the scientific activity and outlining future research perspectives.

The activity reflects the integration of the role of pneumologist clinician with that of teacher and researcher, with the objective of promoting a modern, mechanism-based approach, oriented towards personalized medicine and the academic training of future generations of doctors.