ABSTRACT – HABILITATION THESIS

Innovation and standardization in pathology and pathophysiology: A multidisciplinary model for the medicine of the future

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The habilitation thesis entitled “Innovation and standardization in pathology and pathophysiology: A multidisciplinary model for the medicine of the future” presents my research, academic and professional activity.

Starting from the concept of medicine of the future, I began my academic, research and professional activity after completing my undergraduate studies in medicine at the Faculty of Medicine of the “George Emil Palade” University of Medicine, Pharmacy, Sciences and Technology in Târgu Mureș. I followed both academically (Ph student, assistant professor, lecturer) and professionally (resident pathologist, specialist pathologist) steps in the development of my career.

The concept of my professional development was multidisciplinary, with undergraduate studies in medicine and law, master's studies in healthcare management, medical law and medical humanities, but also in molecular pathology and precision medicine (European Master's Degree in Molecular Pathology - University of Cote d'Azur, Nice, France - in progress). My professional development also went towards the field of quality assurance, both in higher education and in healthcare.

My research strategy was structured on three research directions: Direction 1 - Diagnostic standardization, integration of biomarkers in precision medicine, artificial intelligence and digital pathology in pathology, Direction 2 - Morpho-functional correlations and pathophysiological mechanisms in cardiovascular, respiratory and oncological pathologies, Direction 3 - Integrative pathology: the influence of clinical, epidemiological and environmental factors on diagnosis and prognosis.

The habilitation thesis complies with all national and specific criteria of our university and meets all scientific rigors. Scientific, professional and academic achievements, by thematic directions are presented in detail with references to all my research activity. The 10 representative articles selected for the habilitation thesis represent the special interest for the development of future medicine.

Research direction 1 is structured in 3 research sub-directions: The first sub-direction refers to histopathological foundations and epidemiological perspectives in the standardization of the diagnosis of non-melanocytic skin cancers and addresses the histology and clinical and epidemiological characteristics of non-melanocytic skin cancers from the perspective of the

pathologist. At the same time, the research also refers to the identification of areas of interest on this topic. The approach to basal cell carcinomas and squamous cell carcinomas of the skin is structured, with studies published in research teams adding value to this field. The second sub-direction refers to diagnostic challenges and new paradigms in the pathology of melanoma and melanocytic skin lesions, addressing the topic of melanoma and Spitz lesions. Through an approach based on innovative new markers in the diagnosis of melanoma, the research carried out brings new perspectives in the diagnosis and prognosis of this pathology. The third sub-direction refers to the reconfiguration of the role of the pathologist: between digital pathology, digital analysis augmented by AI and the empathic dimension of the diagnostic act. Thus, research on this topic is part of how artificial intelligence and digital pathology play an increasingly important role in the histopathological diagnosis of skin lesions. At the same time, within this sub-direction, the first study in the specialized literature conducted on the staff of pathology services regarding empathy in the face of the unseen patient and the psychological burden of developing oncological diagnoses is presented. The last research sub-direction is represented by histopathological and molecular profiles of cancer: biomarkers, tumor microenvironment and rare entities. Research on this topic included the study of new diagnostic and prognostic markers in gastrointestinal cancers, rare and newly classified renal tumors and neuroendocrine tumors.

Research Direction 2 entitled Pathophysiological Mechanisms and Determinants in the Development and Progression of Lung Diseases addresses, through the perspective of pathophysiological mechanisms and disease determinants, the mechanisms and clinical consequences of diseases. The direction is structured into 3 research sub-directions. The first research sub-direction refers to pathophysiological mechanisms and determinants in the development and progression of lung diseases. Thus, through the perspective of research on the mechanisms of development of lung diseases, it addresses topics such as the role of inflammation at the pulmonary level, developed pulmonary fibrosis and molecular mechanisms, but also pulmonary oncological pathology and the correlations between them. The research carried out brings value through the character of approaching the issue of lung diseases through clinical pathophysiology. The second sub-direction refers to systemic inflammation - an integrative and predictive pathophysiological mechanism of clinical evolution. Thus, inflammation plays a fundamental role in the pathogenesis of diseases, including trauma, where simple markers of inflammation such as inflammatory cells - neutrophils, lymphocytes, etc., can predict the patient's evolution, and subsequently his prognosis. The research brings added value, based on the pathophysiology of inflammation by using NLR or PLR reports, respectively scores that analyze inflammation to improve the quality of medical care. The third sub-direction addresses the role of inflammation in the pathogenesis of cardiovascular diseases - Inflammation and immune response as fundamental axes in the pathophysiology of cardiovascular diseases. Participating in fundamental research processes in this direction, through digital pathology technologies, research on the evolution of acute myocardial infarction through the lens of inflammation in the infarct area, as well as inhibitors of inflammation brings new premises for the development of treatments that limit the unfavorable consequences on the patient with acute myocardial infarction. At the

same time, the role of perivascular adipose tissue in the pathogenesis of cardiovascular diseases has led to research on the impact it has for this category of patients.

Research Direction 3 entitled Integrative Pathology: the influence of clinical, epidemiological and environmental factors on diagnosis and prognosis and addresses the role of multidisciplinarity in medicine. Integrative medicine is not just a concept, but a premise from which the diagnostic act must start. The research direction is structured into 2 research sub-directions. The first sub-direction addresses the impact of the COVID-19 pandemic and clinical, epidemiological and organizational factors on the diagnosis, prognosis and management of diseases. The COVID-19 pandemic has represented a challenge for health systems globally. Thus, regardless of the field, starting from the histopathological diagnosis of skin lesions to the treatment of children and newborns with COVID-19, the research direction emphasizes the latest pathophysiological mechanisms in COVID-19, but also mechanisms of adaptation to a new normality. The research of this sub-direction has brought concrete results regarding the impact that a pandemic can have on a health system. The second direction approaches the human side of medicine, from the perspective of patients by addressing external and contextual factors in health: from resource management to individual behaviors. The scientific approach to this direction started from public health problems among institutionalized children to medical waste produced by health systems and related legislation.

The research directions, in addition to publishing research results, are supported by research projects (with positions of project director or member) as well as presentations at conferences, participation in specialized courses, guest speaker or motivating and involving students in research.

The habilitation thesis contains a number of 293 bibliographic references that support the research activity and create the premises for new research.

Looking both retrospectively and prospectively, my professional, academic and research path, in addition to being a succession of stages, is also a well-organized strategy for defining a value in the field of future medicine. The three plans – scientific, academic and professional – are the 3 interconnected pillars of a long-term strategy.

I want to build a career that meets current academic standards and that develops new benchmarks for the future, through a scalable ecosystem of research, education and medical practice. The measure of success will be, in addition to the number of publications or completed projects, the direct impact on the communities to which I belong.