

UNIVERSITATEA TITU MAIORESCU DIN BUCUREȘTI

ȘCOALA DOCTORALĂ – DOMENIUL MEDICINĂ

HABILITATION THESIS

**EXPLORING BIOMARKERS AS KEY ENTITIES IN DEFINING
THE MOLECULAR AND THERAPEUTIC IDENTITY OF
CANCER**

CANDIDATE

Assoc. Prof. Laura NECULA, PhD

BUCUREȘTI 2026

ABSTRACT OF HABILITATION THESIS

Fundamental medical research, as the main field in which I have been active for the last 20 years, represents the basis of scientific evolution, contributing to the understanding of the essential biological processes that underlie the functioning of the human body, both in physiological and pathological conditions. Thus, understanding the molecular mechanisms and cellular changes that occur in various pathologies contributes to the identification of relevant biomarkers and innovative therapeutic targets for the development of modern prevention and treatment strategies. Although the results obtained do not always offer immediate applicability, basic medical research creates the essential premises for the progress of translational medicine and personalized therapies, having a long-term impact on the quality of medical care and on public health.

The habilitation thesis "Exploring Biomarkers as Key Entities in Defining the Molecular and Therapeutic Identity of Cancer" highlights the main results of the scientific activity carried out in the last 20 years, while also emphasizing the professional and academic achievements acquired after obtaining the title of PhD in Medicine, in 2013. The fundamental medical research studies carried out during this period represented a continuation of the PhD studies that were completed by defending the PhD thesis entitled "Intracellular Signaling in Malignant Proliferations"

The main direction of the studies aimed at analyzing changes in gene expression that occur at the level of signaling pathways in gastric tumor tissue, in an attempt to open new perspectives in understanding the molecular mechanisms involved in neoplastic transformation, in the progression of gastric cancer and, last but not least, in identifying new possibilities for therapeutic approaches by highlighting new biomarkers.

Currently, the diagnosis of gastric cancers relies on invasive techniques, such as endoscopy, and the use of tumor markers, used in the clinic for early tumor detection, but the specificity and sensitivity of these serum biomarkers are poor and, to date, none of them is unique for the diagnosis of gastric cancer. Therefore, the identification of biomarkers in the early stage of this malignancy is essential for improving diagnosis, prognosis, prediction of recurrence and response to treatment.

Thus, a large part of the projects developed at the Institute of Virology focused on identifying new **diagnostic and prognostic biomarkers**, at the circulating and tissue level, in gastric cancer (COL10A1, soluble PD-L1, KRT17). The results obtained showed that circulating levels of COL10A1 are significantly increased in patients with gastric adenocarcinoma and are associated with an unfavorable prognosis (reduced survival) while soluble PD-L1 expression in patients with resectable gastric cancer is associated with disease progression and tumor PD-L1 expression, thus having potential as a biomarker for response to cancer immunotherapy. Studies have also been conducted to validate molecules such as COL10A1 and KRT17 as potential **molecular targets** in the treatment of gastric cancer. Through in vitro and in vivo experiments that block/activate gene expression, we observed a significant reduction in angiogenesis and tumor growth in the case of KRT17 inhibition or the identification of a close association between increased expression of COL10A1 and the processes of proliferation, migration, invasion and

epithelial-mesenchymal transition at the level of the gastric tumor cell. These studies are important for understanding how gastric tumor cells function, as well as for the future development of diagnostic and prognostic biomarker panels and targeted therapies in gastric cancer.

Continuing my research direction in the field of cancer, I participated in a series of studies in the field of hematology focused mainly on the identification of new diagnostic and prognostic biomarkers in classical Philadelphia chromosome-negative myeloproliferative neoplasms. In this regard, molecules such as DKK-1, which represents a potential non-invasive biomarker for differentiating between subtypes of myeloproliferative neoplasms, or HTR1B with potential as a prognostic biomarker (risk of thrombosis) in patients with myeloproliferative neoplasms, have been identified and tested.

These studies, along with numerous other research in the medical field, which are not included in the habilitation thesis, are the subject of research projects in which I was involved as a project director or member of research teams and were materialized by publishing in extenso in journals with a high impact factor and by presenting at various scientific events.

The habilitation thesis also presents the professional achievements obtained in the activity of scientific researcher at the Stefan S. Nicolau Institute of Virology, an institute of the Romanian Academy, emphasizing the education and professional training, the main research directions developed, the professional prestige and the research management activity. At the same time, the academic achievements are detailed, highlighting the involvement in the training of students, young specialists, researchers and PhD candidates.

The last part of the habilitation thesis presents the career development plans at the scientific, professional and academic levels. In this regard, the main directions of fundamental research are listed, which mainly aim at investigating the tumor microenvironment as an important factor supporting the carcinogenesis process. Strategies for maintaining a professional and academic activity at the highest performance standards are also detailed.

