TEZA DE ABILITARE

ROLUL INFLAMAȚIEI CRONICE ÎN PATOLOGIA ASOCIATĂ ÎMBĂTRÂNIRII

DOMENIUL MEDICINĂ

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ABSTRACT

The habilitation thesis entitled *The Role of Chronic Inflammation in Aging-Related Diseases* reflects the scientific, academic, and professional activity conducted since 2011, when I was awarded the title of Doctor in Medicine, as well as future perspectives in these three fields of activity.

After earning my doctoral degree, I continued to focus on the same research topics, chronic inflammation being the first step in defining the three directions of my habilitation thesis: inflammatory bowel disease, neoplastic diseases, proteostasis and cognitive decline in aging. These constitute Chapters I.1, I.2 si I.3, which summarize my scientific research activity, while Chapter II presents my professional and academic development plan.

Chapter I.1. includes a summary of my scientific, academic, and professional achievements. My research allowed and encouraged students to write graduation theses on inflammatory bowel disease, with particular focus on immunotherapy based on biological products obtained from Trichuris suis ova, the development of experimental colitis for establishing immune mechanisms and treatment, inflammatory mechanisms and the role of the IL-17/IL-23 axis, and the identification of new biomarkers in inflammatory bowel disease.

Chapter I.2 focuses on the role of non-coding RNAs in neoplastic diseases. Key elements include the bidirectional communication between stroma and parenchyma in liver and colorectal cancer, onco-microRNAs and suppressor microRNAs in breast cancer, inflamma-miRs and their molecular targets as modulators of carcinogenesis and metastasis, which act as inhibitors and have implications in personalized cancer therapy, as well as common and specific long non-coding RNAs involved in various types of cancer.

Chapter I.3 *Proteostasis and cognitive decline in aging* refers to the ongoing adjustments of gene expression models of proteins as effectors of cellular senescence, adequately modulated by long non-coding RNAs as “supervisors” of both physiological cellular decline and the proinflammatory secretory phenotype associated with age-related pathological decline. The exact relationship between lncRNAs and proteostasis can be explained phenotypically and molecularly through the interactions between lncRNA and RBP, which are essential for maintaining homeostasis and performing all cellular functions. RNA binding proteins have crucial roles in numerous cellular processes. lncRNA homeostasis (lncRNAstasis) also matches protein modifications in cellular senescence, thus maintaining appropriate quality control (QC). Some lncRNAs indirectly regulate protein levels, thereby influencing the available reserve of miRNA and consequently modifying its turnover and transcription. Conversely, some

lncRNAs interact directly with mRNA to improve or suppress the transcription process, or with proteins to change their half-life.

Aging is associated with the progressive collapse of proteostasis, which is a portmanteau word for protein and homeostasis. It includes concurrent and integrated processes that control protein biogenesis, folding, interactions, and degradation inside and outside cells. The dysfunction of proteostasis, including the dysfunction of autophagy and of the ubiquitin-proteasome pathway is a well-known aging factor that causes age-related diseases (ARD), such as Alzheimer's disease, cancer, and other degenerative diseases. The subchapter *Mild cognitive impairment* aimed to establish the profile of circulating microRNAs as a possible screening tool for the diagnosis of cognitive decline in aging.

As a 2002 graduate of the Faculty of Medicine and a current consultant in Laboratory Medicine, my goal has always been to share the knowledge and experience acquired in daily clinical practice through my teaching activity, as well as to solve challenging situations by conducting in-depth research. I have taught Descriptive, metabolic, and clinical biochemistry lectures, practical courses, and clinical training to first, second and fourth-year students, as well as to master's degree students. I supervised over ten graduation theses, supporting students and encouraging them to choose up-to-date topics connected with my research interests.

The visibility of my diverse academic and research activity is proven by articles indexed in Web of Science, an H-index of 7 in Web of Science and of 9 in Google Scholar, and a cumulative impact factor as first author of WOS articles of 45. I have 309 citations in Web of Science and 519 in Google Scholar.

The concept of personalized medicine highlights the scientific and technological innovations that allow doctors to adapt prediction, diagnosis, and treatment individually, using a personalized approach. The ability to integrate molecular and genomic progress into clinical practice is a major challenge for healthcare systems. Changes in non-coding RNAs caused by chronic inflammation act as a control center for increasing or reducing the expression of genes involved in physiological and pathological aging. The second part of the thesis presents my research, academic and professional perspectives. My main areas of research will continue to focus on the study of subclinical atherosclerosis through genetic and epigenetic studies. My habilitation thesis also includes 249 references used in the research and writing process.