

MULTIDISCIPLINARY PERSPECTIVES ON GLOBALLY RELEVANT DISEASES: EXPERIMENTAL AND CLINICOPATHOLOGICAL INSIGHTS INTO NEUROLOGICAL, CARDIOVASCULAR, HEMATOLOGICAL, AND CONGENITAL DISORDERS

SUMMARY

Chapter I: A significant part of the **postdoctoral scientific work** aimed to capitalize on expertise acquired in using modern techniques developed at the end of the 20th century, such as immunohistochemistry and molecular biology. These techniques were applied to basic research through the design and execution of experimental studies aimed at furthering the understanding of the mechanisms involved in chronic diseases of major interest due to their impact on morbidity, mortality, quality of life, and the associated socioeconomic burden.

I.A. Fundamental Research: Study of Mechanisms Involved in the Evolution of Frame Diseases in Experimental Models

1. **Experimental study of epilepsy:** Research has focused on a chronic in vivo experimental model of kindling epilepsy. This model is based on the hypothesis that high-frequency oscillations, generated by a small volume of brain tissue with morphological and molecular changes associated with synchronized pathological electrical activity, may induce interictal activity. This activity facilitates the consolidation and expansion of epileptogenic networks and the initiation of seizures.
2. **Experimental study of Acute Transient Cerebral Ischaemia:** This work were performed in animal models to analyze the effects of docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid, on the inflammatory response in the brain, spleen, and bone marrow, as well as on the plasma cytokine profile, in the context of transient focal cerebral ischemia induced experimentally
3. **Experimental study of Osteoarthritis:** This study examined the effects of meloxicam, a cyclooxygenase-2 (COX-2) inhibitor commonly used to treat osteoarthritis. The study used a rat model of chemically induced knee osteoarthritis, which was induced by injecting monoiodoacetate (MIA) into the knee joint. The study evaluated the degenerative processes and their impact on joint functionality.

I.B. Clinical, morphological, and molecular studies in vascular pathology

A second priority area of research was **vascular pathology**, with an emphasis on studying **atherosclerosis** and **atherothrombosis** through international collaborations and interdisciplinary projects.

1. **Morphological and molecular study of atherosclerosis:** The research focused on investigating the role of factor XIII (FXIII) in the pathogenesis of atherosclerosis and atherothrombosis. The objective was to identify the cell type in which the cellular variant of FXIII (cFXIII) is expressed and determine its origin (plasma or cellular).

2. **Coronary atherothrombosis:** A detailed histological characterization of coronary thrombi of different ages was performed using morphological and immunohistochemical methods to highlight the presence of activated protein C (APC) and its relationship with neutrophil extracellular trap (NET) components.

The scientific activity of the interdisciplinary research team at UMFST has expanded to include other vascular entities:

3. **Peripheral Arterial Disease and Carotid Atherosclerosis:** These studies aimed to conduct morphological and immunohistochemical analyses of atherosclerotic plaques, differentiated by location (carotid artery versus lower limb arteries), and to correlate these plaques with circulating biomarkers of plaque vulnerability in patients with advanced carotid artery stenosis.

The results have been published in seven ISI-indexed articles, three of which list me as the lead author.

4. **Arterio-Venous Fistula (AVF) in Hemodialysis Patients:** In view of the increased incidence of AVF maturation failure and its negative impact on the survival of dialysis patients, a clinic-morphological and immunohistochemical study was proposed.
 - In the first phase, we assessed the predictive potential of inflammatory biomarkers (NLR, PLR, SII, and CRP), the calcium-phosphorus ratio, and vascular diameters in fistula maturation.
 - In the second phase, histological (van Gieson elastic staining) and immunohistochemical (CD31-positive surface staining to detect evidence of neoangiogenesis) analyses were performed and subsequently correlated with laboratory parameters involved in predicting AVF functionality (SII, NLR, PLR, and IL-6).

I.C. Clinicopathological studies in haematopathology, pediatric surgical pathology, and pediatric oncopathology.

Since 2001, I have worked as a specialist doctor in the fields of surgical pathology and pediatric oncopathology. Since 2005, I have also specialized in hematopathology. These areas are now the main focus of my work as a primary pathologist.

1. **The most important clinical and morphological studies in hematopathology** have focused on the role of certain factors in the prognosis and treatment of acute myeloid leukemia (the prognostic role of the FLT3 gene in AML), chronic myeloid leukemia (the prognostic role of the BCR-ABL gene in CML), and myelodysplastic syndromes (the prognostic role of the p53 gene in MDS). P53 expression and microvascular density in myelodysplastic syndromes; the prognostic role of the FLT3 gene in acute myeloid leukemia; monitoring M-BCR-ABL transcripts to assess response to therapy and detect relapse early in chronic myeloproliferative diseases; the role of angiogenesis in lymphoproliferative diseases; and the role of osteomedullary biopsies in diagnosing, differentiating, and staging lymphoproliferative diseases.
2. The most frequent topics addressed in **pediatric pathology** were tumor pathology, particularly lymphomas and myeloproliferative diseases according to age and histological subtype, as well as congenital malformations that endanger the patient's life and limit therapeutic options, such as malformations of the digestive tract (Hirschsprung's disease) and cardiac malformations.

The most important results have been disseminated through ISI-indexed publications. The author is the main author of 13 and a co-author of 7, all of which are listed in the bibliographical references.

Chapter II: This chapter outlines the professional, scientific, and academic career development plans, highlighting strategic objectives such as enhancing teaching quality and promoting educational excellence. Key goals include fostering excellence in research, education, and interdisciplinary collaboration. Emphasis is placed on innovation, technology transfer, and increasing the visibility of scientific activities through inter-university and international partnerships. Additional objectives involve expanding the number of publications in collaboration with international research groups and actively engaging in the working committees of national and international professional societies.