ABSTRACT

The habilitation thesis entitled "Characterization of tissue reactions produced by some biomaterials and xenobiotics" presents the main scientific, professional and academic achievements in the field of Pathology, from the time of obtaining the PhD degree (2009) to the present, as well as future plans regarding career development, research area and future professional projects.

According to the criteria recommended and approved by the CNATDCU, the habilitation thesis has 3 sections, as follows: ***Section I*** - scientific achievements, in which the main research directions and results obtained, professional and academic achievements are briefly presented. ***Section II*** - career development plan and ***Section III*** - references.

In this period, I have carried out studies on normal and pathological morphology in the following interdisciplinary fields: toxicology, surgery, regenerative medicine, nanomedicine, infectious diseases, mycology and microbiology. In addition to contributing to the proposal, testing and evaluation of new, innovative biomaterials with applications in regenerative medicine, I have participated in the study of toxicity induced by mycotoxins, antibiotics, anti-inflammatory substances on laboratory animals.

The results, representative for the evolution of my own research career, are presented in Section I, Chapter I, and are systematized in three research directions:

(1) Histopathological evaluation of the regenerative effect of some biomaterials on tissues; -design of new biomaterials and their *in vivo* testing;

(2) Biomedical applications of cold plasma discharges on tissues;

(3) Tissue toxicity induced by some xenobiotics.

The results are presented in the context of the current state of scientific research in pathology, highlighting the original contributions and their relevance to the field.

The first direction of research refers to the histopathological evaluation of the regenerative effect of some biomaterials on bone, skin, muscle and nerve tissues and their *in vivo* testing.

The biocompatibility of bone tissue with new biomaterials (alloys), based on magnesium (Mg) and calcium (Ca) enriched with manganese and zirconium, has been studied for their use in bone regeneration, with

applications in orthopaedics and dentistry. The results confirmed that Mn and Zr-enriched Mg alloys are biocompatible and biodegradable, and these properties recommend their use as possible materials for new orthopedic medical devices.

In this research direction we tested *in vivo* the cytocompatibility and functionality of magnetic composites based on chitosan, collagen, hyaluronic acid, in which 5% colloidal solution of magnetic particles made of chitosan-functionalized magnetite was added. The results obtained indicate the possibility of using biomimetic magnetic matrices obtained by a biomimetic co-precipitation process in applications related to bone tissue engineering and regeneration.

Following histopathological evaluation of the regenerative effect of membranes made of bacterial cellulose and keratin enriched with stem cells in skin wounds, skin healing had an excellent results in the regeneration of the damaged structures.

In vivo studies in murine models, on the improvement of flexor tendon gliding by the use of carboxymethylcellulose-polyethylene oxide combination (Dynavisc®), demonstrated the important role of the biological lubricant in regeneration, not only of the tendon, but also of the peritendinous structures, limiting aberrant fibrous proliferation in the regeneration process and helping to build a peritendinous space, which will later form a true synovial sheath.

The method of grafting peripheral nerves by constructing a "muscle-in-vein" graft has had outstanding functional and histopathological results in nerve regeneration. This method, according to the results obtained, is effective and can therefore be implemented in the current treatment of extensive peripheral nerve injuries.

The second line of research presents original studies on biomedical applications of cold plasma discharges on tissues. Our results showed that PAW does not induce functional and histological changes in organs and, moreover, does not cause changes in hematological and biochemical parameters in the blood, indicating no alteration of the homeostasis.

Also, the *in vivo* study of the use of cold plasma at atmospheric pressure (CAP) on skin flap vitality in rats indicates reduced necrosis rate and its regenerative potential.

The third direction of research was the study of tissue toxicity induced by some xenobiotics (kojic acid, patulin, gentamicin, amoxicillin/clavulanic acid), describing the tissue changes, and in the case of gentamicin-induced nephrotoxicity, demonstrating the important protective role of zinc.

In chapter II and III, the most important results of my professional and academic work, which I have obtained after the completion of my PhD thesis till now, are presented.

Section II presents the evolution and development plan of my professional, scientific and academic career, including the proposed objectives and their implementation possibilities.

Section III includes the list of references used in this thesis and the articles included in it.