SUMMARY

1. INTRODUCTION

The habilitation thesis presents the main achievements of my career of more than thirty years, which started and continues today at the "Ovidius" University of Constanța, where I am currently associate professor in Histology, and in parallel with this I work as a practitioner in the Dermatovenerology clinic of the County Emergency Clinical Hospital of Constanța.

The habilitation thesis is structured in three parts: the first part presents the main milestones of my scientific, professional and academic research activity; the second part describes the future plans for evolution and development of my professional career in my specialization field, and the third and last part includes a selection of references consulted for the elaboration of the scientific work.

2. SCIENTIFIC, ACADEMIC AND PROFESSIONAL ACHIEVEMENTS

In the first part of the thesis I have included an overview of the most relevant results of my post-doctoral research activity, which was determined by the multidisciplinary research environment and teams in which I worked, as well as by the acquired personal skills.

Thus, one of the main research directions has been predominantly oriented towards the study of melanoma, another research direction has been oriented towards the valorization of marine resources for the production and use of nanocomposites for therapeutic purposes, and the third major direction is the research oriented towards osteo-articular pathology and specific therapies of physical medicine and rehabilitation.

2.1. Scientific achievements

2.1.1. In 2000 I obtained the title of PhD (Doctor of Medical Sciences) in the University of Medicine and Pharmacy "Carol Davila" Bucharest, for the thesis entitled "Structural, ultrastructural and cytochemical changes in the dermis of the skin subjected to the action of chemical agents", under the direction of Prof. univ. Dr. Doina Onicescu.

2.1.2. Publication of articles and academic books/ participation in research-development-innovation projects

My post-doctoral publishing activity consisted in the publication of 19 articles in ISI impact factor journals (10 as main author, 9 co-authors) and more than 30 articles published in BDI journals, complemented by the publication of 6 Histology textbooks and practical notebooks as main author and 2 academic courses as co-author. I also participated in 8 research - development - innovation projects on a contract/grant basis (in 2 as manager and in 6 as expert member).

Research directed towards the study of melanoma

In cutaneous pathology, the main research topic has been the histologic, immunohistochemical and genetic study of melanoma and the acquired form of familial melanoma.

The first article published in this direction was the result of the research activity carried out in the framework of a grant won by internal competition in which I was a member of the research team. This study characterizes PD-L1 expression in melanoma in the context of T-cell infiltrates, as PD-1/PD-L1 blockade is the target in the therapeutic strategy for melanoma.

I continued my research as project manager in a second research grant won by internal competition, which resulted in the publication of a series of 3 articles in ISI indexed journals.

The first article was an observational study evaluating the correlations between p14 and p16 immunophenotypes and cyclin-dependent kinase 2A inhibitor (CDKN2A) mutations in primary multiple and familial melanoma. The study may represent the starting point for the development of tailored diagnostic and therapeutic algorithms, based on the significant p14-p16-CDKN2A described correlation.

The 2nd published article evaluated the significance of CD8+ lymphocyte CD8+ phenotype in primary multiple and familial melanoma with varied CDKN2A mutational status. The study assesed the accuracy of the classical "naked-eye" counting method of CD8+ T cells existing in tumor and in the peritumoral infiltrate in comparison to the counts obtained by specialized software run with artificial intelligence (AI) - QuPath platform. The conclusion emphasizes that CD8 lymphocyte phenotype is of major significance in familial and multiple primary melanoma and that its assessment may be a cost-effective investigation to help determine the prognosis of melanoma and response to immunotherapy.

The 3rd published article focused on the development of a triple P16-CD8-Ki67 algorithm for the prediction of CDKN2A mutations in patients with primary and familial multiple primary melanoma using immunohistochemical methods to classify multiple primary melanoma (MPM) and familial melanoma (FM) patients according to their mutational status. The study assessed the immunohistochemical status for p16, CD8 and Ki67. The developed algorithm including these three parameters based on their prognostic and developmental significance proves to be a valuable ancillary diagnostic tool for predicting mutational status in the detection of multiple primary and familial melanomas with homozygous CDKN2A deletion.

Research directed towards the production and use of nanocomposites for therapeutic purposes

In this direction I have published two articles as main author. The first one was about the characterization and practical applications of new composite materials obtained by green synthesis technique, through the deposition of zinc oxide on calcium carbonate precipitated in green algae extract.

Obtaining process of the composite materials consisted in the deposition of zinc oxide on precipitated calcium carbonate using a polysaccharide template from green seaweed (*Ulva lactuca*) and which can modify particle morphology and act as cupping agents. The therapeutic effect of the obtained composite material was evaluated *in vivo* for topical treatment of burns.

The level of malondialdehyde (MDA), studied as a marker of oxidative stress showed an increased antioxidant activity of the composite material, compared to ZnO.

This paper has been awarded by UEFISCDI for research results in the PRECISI_2020 competition.

The next article in this series dealt with the use of calcium carbonate as a carrier of silver ions in composite materials obtained in green seaweed extract, for topical applications. An aqueous extract of green seaweed (*Ulva lactuca*) was used for the phytochemical synthesis of silver nanoparticles (AgNPs), which acted both as a reducing agent and as a coating agent. Thus, through a two-step synthesis, two new Ag-AgCl/CaCO3 composite materials with different Ag:CaCO3 molar ratio were obtained in green algae extract. The dermatologic properties of the 2 composite materials were tested "*in vivo*" for burn healing. The results obtained recommend the Ag-AgCl/CaCO3 composites for topical applications.

Research directed towards the study of osteo-articular pathology and specific therapies of physical medicine and rehabilitation

The first article published on this direction presented the conclusions of an "in vitro" experiment with possible implications for clinical practice that evaluated the response to axial and para-axial loading on lumbar vertebral blocks harvested from human cadavers.

The next published article included a systematic review based on the internationally accepted "PRISMA" methodology (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) of multidisciplinary non-pharmacologic treatments with effects on pain modulation and function in spondyloarthropathies.

The most recent article published on this research direction focused on the presentation of clinical evidence on the dynamics of Baker's cyst size after intermittent vacuum therapy as a rehabilitation treatment in patients with osteoarthritis of the knee.

2.2. Academic achievements

My teaching career began in 1991 when I became full-time teacher at the Histology Department of the Faculty of Medicine of the "Ovidius" University of Constanta, where I held the positions of assistant professor (1991-1999), lecturer (1999-2007) and associate professor (2007-present), my teaching activity included lectures and practical works in Histology for students of the study programs Medicine, Medicine with English teaching, General Medical Assistance and Balneofiziokinetoterapie and Recovery.

2.3. Professional achievements

In my professional activity I went through the stages of training in the medical specialty of Dermatovenerology, having as milestones obtaining the title of specialist and then primary Dermatology physician; currently working as head physician of the Dermatovenerology Clinic of the County Emergency Clinical Hospital "Sf. Apostol Andrei" Constanța. I also hold the position of residency coordinator in the specialty of Dermatovenerology.

In parallel, through participation in numerous training courses, I have also obtained competence in Dermato-cosmetology.

3. CAREER DEVELOPMENT PLAN

The 2nd part of the habilitation thesis presents the career development directions that I intend to pursue in the future. These will basically continue the directions followed so far, which can be further developed and deepened. In this sense, the skin pathology represented by melanoma, as well as the utilization of coastal resources, remain landmarks for the future.

3.1. Research career development will be oriented towards:

- a thorough understanding of the molecular and genetic mechanisms of melanoma;
- epigenetic studies of melanoma and the role of various types of non-coding RNA in melanoma onset and progression;
- the use of artificial intelligence (AI) in the diagnosis, evaluation of the efficacy of therapeutic regimens and the prognosis of melanoma progression;
- the exploitation of marine resources with applications in the medico-pharmaceutical field will continue towards the identification and characterization of new specific bioactive compounds from marine green algae (sulphated polysaccharides, carotenoids and polyphenols) with antioxidant, anti-inflammatory and antimicrobial properties;
- of research interest remains the identification and description of the molecular mechanism by which these compounds may interact with integumentary cells to restore normal skin metabolism and/or to improve skin regeneration mechanisms.

For the implementation of the research activity I plan to continue to participate in the elaboration and submission of projects in order to access grants that will provide the necessary financial resources.

I also consider important to continue the collaboration in interdisciplinary teams, including both young researchers, doctoral students and experienced teachers, because this way important research results can be obtained, results that can be capitalized by publishing scientific papers in refereed journals, indexed in international databases.

3.2. Academic development - The main directions of academic development are:

- participation in national and international academic exchange programs
- development of academic books and courses, among which I would like to mention: Histology - Lecture notes for medical students, as well as General and Special Histology - Atlas and text with electronic support, projects already started in collaboration with my colleagues from Histology department. In addition, in the near future, I plan to develop a Histology Technique Guide.

3.3. The development of my professional career will continue on the one hand through participation in prestigious national and international events (postgraduate training courses, congresses, conferences), and on the other hand it will continue in the direction of deepening collaborations with recognized centers in the field of Dermatology, as well as interdisciplinary local, national and international collaborations.