UNIVERSITY OF MEDICINE AND PHARMCY "CAROL DAVILA" BUCHAREST

DOCTORAL SCHOOL MEDICINE DOMAIN

Contributions to the management of allergic diseases in the era of precision medicine HABILITATION THESIS ABSTRACT

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The habilitation thesis entitled "Contributions to the management of allergic diseases in the era of precision medicine" was elaborated in accordance with the recommendations of the National Council for Attestation of University Degrees, Diplomas and Certificates and the C.S.U.D. regulations of the "Carol Davila" University of Medicine and Pharmacy in Bucharest regarding the obtaining of the habilitation certificate, and includes a brief display of the evolution of my career from a professional, academic and scientific point of view. The most important scientific contributions made after obtaining the title of Doctor of Medicine in 2007 are particularly highlighted. Personal data are presented in relation to those in the specialty literature, emphasizing the originality of the research projects and the contribution of our pursuit in current fields. Also, the main directions of academic, scientific and professional career development are presented. The habilitation thesis is structured in three important sections (except for the bibliographic references).

The first section contains identification data. I am an Associate Professor, Head of Discipline, Allergology Discipline, Clinical Hospital of Nephrology "Dr. Carol Davila", Clinical Department 3; Allergology Compartment Coordinator, Clinical Hospital of Nephrology "Dr. Carol Davila"; Allergology and Clinical Immunology Residency Coordinator, Bucharest University Center; senior physician in allergology and clinical immunology with overspecialization in pediatric immunology and allergology and dermatovenerology specialist. I went through all the stages of academic education starting from the status of assistant professor, obtained through a contest. I was in the first generation of specialists in allergology and clinical immunology (allergology had previously had the status of overspecialization); I invested a tremendously in my training and that of my residents in an extremely dynamic specialty; In time, I became a landmark in allergology training and specialized practice, with recognition from both colleagues in other specialties and internationally.

The second chapter refers to "Professional, academic and scientific achievements", with three distinct sections, for each of the three activity fields. The experience gained in the three decades of medical, research and teaching activity is mentioned.

After 2 professional stages carried out in the Nicolae Malaxa Clinical Hospital (here I started my activity under the coordination of Prof. Dr. Dr. Jeana Rodica Radu) and SUUE (here I

laid the foundations of the first Allergology Department in an emergency hospital), since 2018 I am the Coordinator Of the Allergology Department within the Clinical Hospital of Nephrology "Dr. Carol Davila". The third stage of the professional activity of allergist is focused on obtaining national and international recognition of this tertiary center as a reference (excellence) one for drug allergy and monitoring of biological therapies in allergic diseases (cutaneous and respiratory), the 2 areas which comprise the excellence niche of my professional and scientific contributions in recent years.

Involvement in promoting the importance of the specialty of allergology and clinical immunology, its practice landmarks, recognition of the role of "ambassador" of the specialty in relation to other specialties, determined my election as President of the Professional Scientific Society, Romanian Society of Allergology and Immunology Clinic (RSACI) during 2017-2021, after the previous vice-president position. I am a member of honor of RSACI and RSP (Romanian Society of Pneumology). I coordinate the RSACI working groups on drug allergies and biological therapies.

I am currently the RSACI representative at EAACI (European Academy of Allergology and Clinical Immunology) and WAO (World Allergy Organization). I am a national coordinator of HEAD REGISTRY, a project initiated by EAACI for the national implementation of the registries of the main allergic diseases (rhinitis, asthma, atopic dermatitis, chronic urticaria, drug and food allergies).

At the same time, I hold the position of vice-president in the Consultative Commission of Allergology and Clinical Immunology of the Ministry of Health, and in that of the Romanian College of Physicians. I have been a member of most of the specialty exam commissions since 1999, and since 2018, chairperson of the specialty or exam commission in allergology and clinical immunology. I was a member of the PHD examination Committees.

Since 2018, I have been the holder of the optional course "Allergic Emergencies" for fifth year medical students, the optional course "Essential Allergology in Dentistry" for sixth year dentistry students and the optional course "Essential of Allergology" for third year Midwifery and Nursing University students. Starting with the academic year 2021-2022, I am also responsible for the course of the Scientific Research Methodology (SRM) for the 4th year of medical students; the compulsory module of allergology (course and practical work) for the 4th year dentistry students was also approved, in accordance with the new ARACIS norms.

The training of students and residents, both theoretical and practical, has always been a priority to me. I tried to build the courses in an attractive didactic way (I also went through

a few modules such as training of trainers) always asking for feedback, which I incorporated in the subsequent presentations. Being a clinical specialty, we prioritized the exercise of case presentations, in different formats, including in online format on clinically constructed cases. I organized the exams of the students and the stage exams of the residents (allergists, pulmonologists, dermatologists, occupational medicine residents) and I guided them in choosing the topics and participating in various scientific events. I have guided and will continue to guide students in achieving their license thesis. I participated in all the admission competitions for the Faculty of Medicine, for the residency competitions for which I was requested.

We have collaborated in the development of educational projects: e-learning module on severe asthma (e-asthma), management of anaphylaxis (action plan in anaphylaxis), management of drug hypersensitivity reactions, recommendations on vaccination against SARS-CoV2 in allergic patients. Every academic year I have post-graduate training courses for allergists (3-4 / year), at least 2 being in the field of drug allergy, my field of excellence and connected to the concerns of the clinical department in which I work. I have participated in most European Allergology Congresses (including moderating some sessions) and organized EAACI symposia at SRAIC National Conferences and Congresses (in 2017, 2019 and 2021). Most of my former residents also passed the European allergist exam (organized every year by EAACI), proving once again the quality of training in allergology. I have given guest presentations at numerous national and international conferences and congresses. I have represented in recent years and continue representing the position of allergology in Romania within the European Academy of Allergology and Clinical Immunology and the World Allergology Organization.

Throughout the entire period following his doctoral dissertation, I have published 28 articles in ISI Thomson Reuters indexed journals (16 articles as main author and 12 articles as co-author). At this time the Hirsch index is 7. 35 abstracts of papers presented at international conferences that have been published in ISI journals. 12 articles were published in pubmed indexed journals and 8 in CNCSIS B (+). I was a grant director in 2 projects (1 international and 1 national) and a member of the research team in 2 national and 1 international projects (GA2LEN- European Network of Excellence). I have been a principal investigator in 11 international studies and a co-investigator in 7; I was a national coordinator in an international multicenter study. I was a member of 2 international research teams (ARIA working group and Bilastine working group) that generated numerous publications. I reviewed scientific articles for 7 publications (including Allergy with IF-13,146) and I was

the editor in chief of the Alergologia journal (RSACI magazine) during the term of RSACI President (2017-2021). I have been a member of the editorial board of the Alergologia journal since its inception.

Recently, research efforts have been concentrated on 3 important directions/areas: the management of respiratory allergic diseases (focusing on molecular diagnosis and allergen immunotherapy), the management of drug-induced hypersensitivity reactions and the management of allergic skin conditions (focusing on each of atopic dermatitis and chronic urticaria).

In each of these 3 subchapters, the contributions that our research has made in each of these fields are presented in detail in the thesis. I analyzed the results of the main publications (original articles, reviews, but also presentations of special cases, with elements of innovation) with relevance in the areas discussed. In addition, the results of an educational grant for atopic dermatitis have been detailed, with a major impact on the education of the physicians and involved/affected patients.

The third section of the habilitation thesis refers to the future directions of professional, academic and research career development.

From a professional perspective, I propose permanent improvement, increasing the level of training, in terms of developing medical knowledge, as well as educational skills and research ability. I undertook ongoing online medical education programs, an updat course in medical statistics but also public health and health management courses. The field of molecular allergy is a new and dynamic one; It requires a constant development with newly discovered allergen components and their significance in day-to-day clinical practice.

From an academic standpoint, I aim to build interactive and attractive courses on a regular basis and to organize regular case presentation workshops and discussion sessions of the results obtained by junior researchers.

Allergology has become an indispensable discipline for the training of medical students (as specified in the current ARACIS rules), given that at present 1 in 3 subjects may be allergy sufferers. We teach essential concepts of Allergy to students of Medicine, Dentistry and Midwifery and Nursing. We also included the main allergic emergencies as

well as modern notions related to the management of drug-induced hypersensitivity reactions. We hope that in the near future we will coordinate an allergy module (courses and practical classes) in the training of medical students. We invest a great deal of enthusiasm and energy in the interaction with our students; many of them choose allergological themes for their license thesis and "Allergology and Clinical Immunology" speciality after completing the course of our discipline. We aim to make this course more attractive every year, by introducing current concepts of molecular biology and fundamental immunology, essential to any speciality selected by the student, future doctor. I also proposed to extend the discipline of Allergology, including future young PhD students. I am confident in the potential offered by my younger colleagues in developing a discipline as dynamic as the Allergology discipline.

The postgraduate courses in the area of drug allergy will continue in the way we have launched them: with beginners and advanced modules. Those who enroll in these courses are allergists from all university centers, thus consolidating the prestige of our center as a reference center in national training in the area of drug allergy and the prestige of the "Carol Davila" University of Medicine.

Developing scientific research skills is another objective; I aim to improve the knowledge of biostatistics, strengthen interdisciplinary collaborations and initiate new ones, preserve and develop the already established international connections. The work of EAACI's ARIA-Allergic Rhinitis and its Impact on Asthma Expert Group (in which I have been active for 3 years) is extremely fruitful, generating many and annually publications in journals with a very high IF Thomson Reuters (Allergy has an IF of 13,146).

I further propose to initiate and participate in national and international research projects, in which as many of current and future colleagues from the clinic will be involved, who can ensure the maintenance of the high standard of our clinic and discipline but also the fulfillment of the promotion criteria.

The main future research directions will continue the current concerns and will include:

- Study of the epidemiology and risk factors involved in hypersensitivity reactions induced by the 3 main groups of drugs: Beta-lactam antibiotics, NSAIDs and iodinated contrast agents; particularities in different age groups
- Development of desensitization protocols in complex clinical situations, in which the respective drugs are indispensable
- Application of international protocols for intensive in vivo allergic evaluation (skin tests and challenge tests) of drug-induced hypersensitivity reactions in patients with a one day hospitalization but with special monitoring conditions; development of a monitoring and research center of the "interventional allergy" type, a pioneering concept in Romania
- Creating an interdisciplinary team of allergy-anesthesiology type within our hospital for the
 adequate evaluation of perioperative anaphylaxis cases and the publication of original works
 on series of cases; allergists will go through intensive pharmacology modules of general
 anesthetics (pharmacokinetics and pharmacodynamics) and anesthetists will go through the
 modules of allergy to anesthetics
- Creating an extensive database of uniformly evaluated patients with drug-induced hypersensitivity reactions; publishing original papers or reviews in journals with high IF Thomson Reuters and presenting results at national and international meetings; we intend to apply (after meeting the established criteria) for obtaining the WAO (World Allergy Organization) Excellence Center qualification
- Research of the autoimmune mechanisms involved in spontaneous chronic urticaria but also
 of the peculiarities of therapeutic response (including biological therapies); we will apply
 (after meeting the established criteria) to become a reference center in the GA2LEN network
 of excellence (UCARE)
- Evaluation of biomarkers potentially correlated with the response to biological therapies in severe clinical forms of chronic urticaria and atopic dermatitis
- Applicability studies of the novel allergen molecular markers in the diagnosis of respiratory allergies
- Studies evaluating the effectiveness of immunotherapy with allergen vaccines (essentially sublingual) in special populations of allergic asthmatics

I have the duty to capitalize on the chances, to expand the research team, to stimulate creativity, but maintaining the rigorous and correct working style, for the scientific and academic prestige of my discipline and of the UMF "Carol Davila".