

UNIVERSITATEA TITU MAIORESCU DIN BUCUREȘTI

ȘCOALA DOCTORALĂ – DOMENIUL MEDICINĂ



HABILITATION THESIS

-SUMMARY OF THE THESIS-

ELEMENTS OF DERMATOLOGICAL IMMUNOLOGY TRANSLATED INTO CLINICAL PRACTICE

FIELD: MEDICINE

Candidate

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The habilitation thesis entitled “Elements of Dermatological Immunology Translated into Clinical Practice” synthesizes the main scientific, academic, clinical, and institutional achievements developed throughout my university and professional career, with particular emphasis on the activity carried out after completion of my doctoral thesis. The unifying thread of this entire trajectory is the translation of advances in immunology and cell biology into a better understanding of the mechanisms underlying dermatological diseases, the identification of relevant biomarkers, the optimization of therapeutic decision-making, and the development of interdisciplinary models of patient care.

My research activity began in the field of cutaneous lupus erythematosus, the subject of my doctoral thesis completed in 2007 in collaboration with the University Medical Center Hamburg. Research on keratinocyte apoptosis, autoantigen exposure, anti-C1q antibodies, complement activation, and pro-inflammatory cytokines contributed to shaping a view of the skin not merely as a target organ, but as an active immunological compartment capable of reflecting early mechanisms involved in the loss of immune tolerance. An important component of this stage was the investigation of the Th17/IL-17 axis in cutaneous lupus and the demonstration of the involvement of IL-17A in lupus-associated cutaneous inflammation. My participation in the European Society of Cutaneous Lupus Erythematosus (EuSCLE), in multicentre projects, and in the development of European therapeutic recommendations represented the translation of this research into standardized clinical assessment and management.

The experience gained in the study of classical autoimmunity provided the foundation for extending my research toward immune-mediated inflammatory diseases, particularly psoriasis and psoriatic arthritis. In this context, one of the important conceptual contributions of my work was the early support of the idea that psoriasis should not be regarded exclusively as a skin disorder, but rather as the visible expression of a systemic psoriatic disease. In a paper published in 2013, I argued for the unified nature of the disease, in which cutaneous, articular, and multiorgan manifestations represent different expressions of a shared genetic, immunological, and inflammatory substrate.

In this thesis, psoriatic disease is analyzed at the interface between autoimmunity and autoinflammation. The association with HLA-C*06:02 and ERAP1, the identification of the autoantigens LL-37 and ADAMTSL5, clonal expansion of CD8+ T lymphocytes, regulatory T-cell dysfunction, and persistence of tissue-resident memory T cells support the existence of a predominantly T-cell-mediated autoimmune component. In parallel, the involvement of keratinocytes, neutrophils, and innate immune mechanisms supports the classification of psoriasis within the spectrum of immune-mediated inflammatory diseases and explains the continuous interplay between autoimmunity and autoinflammation.

A major direction of my research has focused on the dynamics of inflammation and autoimmunity in psoriasis through the assessment of biomarkers readily available in clinical practice, including C-reactive protein, erythrocyte sedimentation rate, the neutrophil-to-lymphocyte ratio, and antinuclear antibodies. These investigations were aimed not merely at identifying laboratory abnormalities, but at integrating biomarkers with the clinical phenotype, comorbidities, therapeutic exposure, and the risk of joint involvement. This approach supports a transition from an exclusively morphological assessment of disease toward a multidimensional evaluation of inflammatory activity.

In this regard, studies conducted in patients with psoriasis have confirmed my sustained involvement in this field. The Romanian Society of Dermatology (SRD) grant awarded in 2024, the paper presented in New Delhi at FIMSA, for which I also received a travel grant, the numerous presentations delivered as an invited speaker at conferences, congresses, and symposia, as well as the many published articles, demonstrate both my interest in this therapeutic area and my commitment to understanding the mechanisms underlying these diseases. The presentation delivered in July of this year at the International Conference on Dermatology and Integrative Skin Care in Taipei, entitled “Concept AI in Dermatology: Transforming the Management of Autoimmune and Autoinflammatory Disease,” is consistent with this conceptual direction.

Interdisciplinary communication represents a particular area of interest in patient management. At Colentina Clinical Hospital, this has been developed through the

establishment of the Multidisciplinary Committee for Complex Cases and the Autoimmunity Board, which bring together dermatologists, rheumatologists, and physicians from other related specialties with an interest in autoimmunity and autoinflammation. The most recent project launched this year is the Journal Club, a meeting format in which experts, residents, and students discuss topics of interest, updates, and innovative ideas concerning disease mechanisms and treatment. Such meetings are intended to stimulate creativity and innovation in disease research, from genetic background to clinical manifestations. The Diploma of Excellence and the Award for Modern Treatments in Autoimmune and Severe Dermatological Diseases, presented at the 2025 Capital Healthcare Performers Gala, recognize these sustained efforts over the years.

The transition from cutaneous psoriasis to psoriatic arthritis constitutes another central axis of my activity. Because cutaneous manifestations frequently precede joint involvement, dermatologists have a genuine “window of opportunity” for identifying patients at risk. Screening for musculoskeletal symptoms, enthesitis, dactylitis, and axial involvement, assessing cutaneous sites with predictive value, and establishing early collaboration with rheumatologists may allow disease recognition before irreversible structural damage develops. This perspective has been translated into presentations at scientific meetings and, most importantly, into prospective research through the GRAPPA-endorsed multicentre COMPOSITION study, which compares screening using the PEST questionnaire with a musculoskeletal examination performed by the dermatologist and subsequently integrates rheumatological assessment and biological sample collection. The study also provides a basis for developing an integrated dermatology–rheumatology model for psoriatic disease.

Interdisciplinary collaboration between dermatologists and rheumatologists is also reflected in my activity within GRAPPA, where, as the only dermatologist serving as a representative member from Romania, I participate in the development of international projects and recommendations for psoriatic disease and related areas. I am currently involved in the process of updating treatment recommendations for psoriatic disease, as well as in OMERACT and IDEOM, initiatives concerned with outcome measures and objective assessment across

rheumatological and dermatological diseases. I have also contributed to the committee working on a new definition of pruritus/prurigo, with a related manuscript currently in preparation for publication. As an elected member representing Romania within UEMS, I seek to contribute to the development of dermatovenereology and to bring a Romanian perspective to the field of autoimmune diseases.

Biological and targeted therapies are analyzed in this thesis beyond their immediate efficacy on cutaneous lesions. Research on the IL-23/IL-17 axes, treatment persistence, primary and secondary treatment failure, paradoxical reactions, and heterogeneity of therapeutic response progressively led to the question of whether treatment can modify the biological course of the disease itself. In this context, the concept of disease modification occupies a central place. Achieving PASI 90 or PASI 100 represents a major clinical objective, but does not in itself demonstrate disappearance of the biological substrate of disease. Clinically healed skin may retain tissue-resident memory T cells, transcriptomic and epigenetic alterations, and a predisposition to recurrence. True disease modification requires control that extends beyond skin clearance and includes reduction of residual inflammation, prevention of progression to psoriatic arthritis and structural damage, control of systemic inflammation and comorbidities, and, ideally, maintenance of biological benefit beyond the period of active treatment.

A substantial number of my presentations at scientific meetings have addressed this complex and highly current topic, as reflected in my curriculum vitae.

This perspective has led to a deeper exploration of tissue immune memory, tissue-resident memory T cells (TRM), T-cell exhaustion, cellular plasticity, and epigenetic mechanisms. The thesis proposes the integrative concept of “inflammatory noise” to describe persistent, sometimes subclinical biological activity that may continue after the visible lesion has disappeared. Interactions among immune cells, keratinocytes, fibroblasts, and adipocytes, together with epigenetic memory, metabolic inflammation, and the microbiome, may maintain susceptibility to recurrence and systemic progression. Thus, clinical remission and biological remission are not necessarily equivalent.

Another direction integrated into the thesis is immunometabolism and metaflammation, a topic extensively discussed with experts from related fields during interdisciplinary scientific meetings. Adipose tissue is approached as an active endocrine and immunological organ capable of sustaining systemic inflammation through adipokines and pro-inflammatory cytokines. The bidirectional relationship between obesity, inflammation, and psoriatic disease contributes to explaining its association with metabolic syndrome and cardiovascular risk and supports the need to assess the patient beyond the extent of cutaneous involvement.

The translational model is extended to atopic dermatitis and other immune-mediated dermatological diseases. Research on disease burden, skin-barrier dysfunction, the microbiome, and non-invasive biomarkers supports a move toward precision dermatology. Integrating tape stripping with the assessment of cytokines, barrier proteins, lipids, keratinocyte and microbial DNA, and microbiome profiles may enable the definition of molecular endotypes, prediction of flares, and monitoring of therapeutic response.

The academic component of the thesis is built around an integrative, interactive, and participatory educational model that connects molecular mechanisms with clinical phenotype and therapeutic decision-making. Students and residents should be able to reconstruct the pathway from the triggering factor to cellular alteration, endotype, local inflammation, clinical phenotype, and systemic involvement. The Journal Club, evidence-based medicine, participation in registries and prospective cohorts, and the critical and responsible use of artificial intelligence are integrated into this model. Mentoring students, residents, and young specialists represents the foundation of my future doctoral supervision activity.

Future directions coherently continue my previous scientific trajectory and focus on identifying biomarkers of the PsO–PsA transition, characterizing residual inflammation and TRM/TEX populations, exploring inflammatory and epigenetic memory, developing non-invasive biomarkers, defining deep remission, and using artificial intelligence to integrate clinical, biological, and imaging data into interpretable predictive models. Consolidation of the interdisciplinary dermatology–rheumatology autoimmunity center and board at Colentina

Clinical Hospital will provide the infrastructure required for the development of prospective cohorts, multicentre projects, education, and translational research.

As Medical Director of Colentina Clinical Hospital, and building on the major advantage offered by its multidisciplinary profile, my priorities include the development of multidisciplinary teams and the promotion of research, clinical studies, and innovation in general.

Overall, the thesis reflects an evolution from the study of classical mechanisms of autoimmunity toward an integrative perspective on immune-mediated dermatological diseases. The element of continuity is the effort to translate immunological mechanisms into clinical benefit: from cell to patient, from biomarker to therapeutic decision, and from control of the visible lesion to prevention of systemic progression. The future objective is to develop an omics-based precision dermatology capable not only of treating clinical manifestations, but also of identifying patients at risk at an early stage, intercepting disease progression, and ultimately contributing to modification of its biological trajectory.