REVIEW

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Member of the scientific jury with Order № 1280 / 04.06.2020 of the Rector of the Thracian University, Stara Zagora

Of dissertation for obtaining the scientific degree "Doctor of Sciences" at Department of Dermatovenereology", Thracian University, Stara Zagora, in the field of higher education 7. Health and Sports, Professional field 7.1 Medicine ,Specialty: Dermatology and Venereology - 03.01.21

To Assoc. Prof. Dr. Razvigor Borislavov Darlenski, Ph.D. Associate Professor at the Department of General and Clinical Pathology, Forensic Medicine, Deontology and Dermatovenereology, Faculty of Medicine, Thracian University, Stara Zagora

Topic of the dissertation: "Structural and functional adaptation of the epidermal barrier after birth and during childhood"

The review of the presented dissertation work of Assoc. Prof. Dr. Razvigor Darlenski was performed on the basis of several criteria corresponding to this type of research and evaluation under Annex 8.3 "Minimum national and additional requirements to the scientific and teaching activities of candidates for the acquisition of scientific Doctor of Science degree.

I. General presentation of the procedure and the doctoral student

The presented set of materials on paper and electronic media is in accordance with the requirements of, the Regulations for development of the Academic staff at the Thracian University under the procedure for acquiring the scientific and educational degree "Doctor of Sciences" at TrU-Stara Zagora. The scientific materials: dissertation, abstract, publications and citations meet the scientometric requirements for science degree "Doctor of Science".

The procedures are legally followed. I am convinced that dissertation proposed for review was prepared by Assoc. Prof. Darlenski. The candidate has submitted a curriculum vitae, as well as diplomas for completed education and acquired scientific degrees.

In 2005 he graduated Medicine at the Medical Faculty, Medical University-Sofia with an excellent diploma. As a trainee doctor in 2004 he did Business Master Class in Pharmacy and Healthcare and Professional Exchange in Dermatology at the University Clinic of Dermatology and Allergology "Schwabing", Technical University, Munich, Germany.

Admitted as a full-time doctoral student in the Department of Skin and Venereal Diseases, Medical University-Sofia in the period 2006-2010. In 2010 he specialized in the University Clinic of Dermatology, Venereology and Allergology, Ludwig Maximilian University, Munich, Germany with a scholarship from the Bulgarian Dermatological Society.

Conducts various educational courses in skin microbiology, non-invasive research methods in dermatology, nanotechnology in medicine, allergic diseases in dermatology, imaging, pharmacology, biological agents in dermatology.

In 2010 he receives a specialty in Skin and venereal diseases and obtained the scientific degree "Doctor" after successfully defending his dissertation on "Clinical and experimental studies on the role of the epidermal barrier in contact hypersensitivity and skin irritation."

Since 2014 he has been an Associate professor at the Department of Dermatology and Venereology, Medical Faculty, TrU, Stara Zagora. Carries out teaching and scientific-experimental activity with exceptional activity and high scientific impact factor of its publishing activity. For 2019 he received from the Thracian University a prize for the highest University publishing activity in international publications in Scopus and Web of Science.

He has 124 scientific publications in reference editions and monographs. Assoc. Prof. Darlenski has participated as an invited lecturer in plenary reports in numerous international and national forums in dermatology and venereology, as well as in allergology.

Since 2013 he has been a participant in the European scientific network EU Cost TD1206 - Development and implementation of European Standards on prevention of occupational skin diseases.

Member of EPOS (European Initiative for the Prevention of Occupational Skin Diseases) at EADV. Participates in 9 research projects, 7 of which are Principal Investigator.

Organizer and participant in National campaigns for diagnosis and prevention of allergic skin diseases and schools for patients and parents of patients with atopic dermatitis, organizer of schools for doctoral students and specialists in dermatology and venereology. Member of the Board and Secretary of BDD.

Assoc. Prof. Darlenski is a reviewer of international scientific periodicals such as: Dermatologic therapy, Archives of Dermatological Research, Dermatology ,JEADV ,Skin pharmacology and physiology,Regulatory Toxicology and Pharmacology; Household and Personal Care Today.

II. Relevance and significance of the research problem.

The dissertation is of modern and essential practical significance. Tracking the physiological adaptation of the human skin barrier after birth is a problem that has excited the scientific

dermatological community. For the first time worldwide, the microscopic and electron microscopic maturation of the epidermal barrier after birth is considered.

Data from Raman spectroscopy for determining the microcomposition of the stratum corneum and epidermis in childhood are presented. Impaired barrier functions of the skin appear at different ages after birth with manifestations such as atopic dermatitis, sensitive skin, irritant or allergic contact dermatitis. These diseases are also a socially significant problem due to their increase, difficulties in professional activities and deteriorating quality of life.

III. Scientific and methodological justification of the problem.

The candidate's familiarity with the problem is evident from the review of the dissertation, which includes 113 literature sources, most of them from the last 5 years, all from international scientific journals.

The literature review is very detailed, well-structured, shows high awareness of the candidate and testifies to the possibility of proper analysis of the problem associated with the maturation of the epidermal barrier after birth and in children. The purpose of the dissertation is clearly stated. The set 8 tasks are specific and can lead to its achievement.

Modern research and statistical methods are used with very good visualization and graphical design of the results. The research methodology allows achieving the set goal and obtaining an answer to the tasks solved in the dissertation, with the possibility that the results are real and objective.

IV. Structure and design of the dissertation

The dissertation is located on 102 pages. It is illustrated with 34 tables, 15 figures and 7 tables. The work contains an introduction, a literature review, a goal and tasks, and in 3 separate chapters are presented their own studies with independently arranged: literary annotation, material and methods, results. A summary discussion is presented in Chapter 5, followed by Chapter 6 - Derivatives. The contributions presented in Chapter 7 are divided into scientific-theoretical (5) and scientific-practical, (5) in number. The conclusions made correspond to the tasks set in the dissertation.

V. Representativeness of the study. Results and interpretation.

The in-depth analysis of the problem and the correct and detailed data about the participants in the research and the methods used in each of the studied topics are impressive. Much of the research has been done in Bioskin, Berlin, Germany, which confirms the international

significance of this scientific work. Modern methods such as Raman spectroscopy, immunoelectron microscopic approach combined with corneodesmosomal analysis, skin imprint method, foreskin biopsies, in vivo confocal microscopy, fibrillar functional immunohistochemistry, biomechanical evaluation were used in each of the chapters of their own studies. The system used to evaluate the electron microscopic isotropy of the skin surface, as well as the use of confocal microscopy, is extremely original.

The selection of participants in the various studies with very detailed data on age and time of the studies is very well justified.

Various statistical analyzes were used such as Statistical Analysis System (SAS Inc., Cary, NC), version 9.1.3, SPSS 12.0, with tests and descriptive statistical methods for reporting the results.

The discussion includes the confirmatory results with the literature data on the problem as well as the results achieved for the first time. Hypotheses have also been made that point to recommendations for the treatment of the skin of newborns in the first days of birth, such as adequate hydration, avoidance of alkaline soaps and detergents. The limiting problems of the study are also presented, such as the relatively low number of children in the analyzed age group.

Also interesting is the first attempt at a semi-quantitative approach to non-invasive evaluation of scanning EM images in the stratum corneum as evidence that the corneocyte surface is a marker for stratum corneum maturation and that the structural and functional adaptation of the skin barrier also involves dermo- the epidermal border and the dermis.

The results are well presented and very original illustrated with tables, figures and photos. The performed analyzes logically follow the goal and the set tasks and are summarized in concrete conclusions. The results in the differentiation of the 3 phases of development of the skin physiology related to the mechanical stability of the skin are very well summarized: the phase of early development, the phase of stabilization and the phase of completion.

The conclusions -11 are short, clear, well formulated and correspond to the results.

VI. Contributing value of research work to the theory and practice.

The contributions in Chapter 7 are presented as scientific-theoretical and scientific-practical, clearly distinguishing those of a confirmatory nature and innovative ones. I accept all contributions without 7.1.1, which I accept as a conclusion. I define as the most significant contribution 7.2.5. for the three-stage practical model for maturation of the epidermal barrier in childhood.

VII. Abstract

The abstract is 34 pages long. It contains all the necessary parts of the dissertation, including the conclusions and contributions. The abstract also reflects a list of scientific papers in connection with the dissertation, not participating in previous competitions for the position of "associate professor" and degree "doctor":

Of the publications presented by the author -5 are in referenced international publications in Scopus and Web of Science, with impact factor, 6 in Bulgarian periodicals and 2 chapters in monographs in English. The publications are in the field of the dissertation. There are no deviations from the text of the dissertation

VIII. Recommendations

The research made in the dissertation is the basis for deepening, expanding and deploying new research. I recommend to continue and expand research on the topic in Bulgaria, making a comparative analysis of indicators such as oxidative stress and the role of cosmetic care and the **social environment on the adaptation of the barrier function of the newborn and the child.**

IX. Conclusion

I believe that the dissertation on the topic: "Structural and functional adaptation of the epidermal barrier after birth and during childhood" contains scientific, scientific and applied results, which represent an original contribution to science in the international aspect and for Bulgaria. They have interdisciplinary significance for various fields in medicine such as dermatology, pediatrics, physiology, etc.

It meets all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for implementation of ZRASRB and the Regulations of TrU-Stara Zagora.

The scientific materials: dissertation, abstract, publications and citations cover the scientometric requirements for science degree "Doctor of Science" according to Appendix 8.3. of the Regulations for development of the Academic staff at the Thracian University.

The dissertation contains theoretical summaries and solutions of major scientific and scientific-applied problems that correspond to modern achievements and represent a significant and original contribution to science.

Due to the above, I confidently give my positive assessment of obtaining the educational and scientific degree of "Doctor of Science" of Assoc. Prof. Dr. Razvigor Darlenski.

25 August 2020

Prof. Dr Evgeniya Hristakieva, DM, PhD