

## Statement

МЕДИЦИНСКИ УНИВЕРСИТЕТ  
ПЛОВДИВ  
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by Assoc. Prof. Nadia Lyubomirova Petrova PhD

Head of Laboratory of "Thermochemistry"

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Concerning dissertation for acquiring the Scientific Degree "Doctor of Sciences"

**Area of higher education:** 7. Healthcare and sport

**Professional field:** 7.2. Dental Medicine

**Scientific specialty:** Therapeutic Dental Medicine

**Author:** Prof. Dr. Neshka Atanasova Manchorova-Veleva, PhD

Department of "Operative Dentistry and Endodontics", Faculty of Dental Medicine, Medical University – Plovdiv

**Topic: "Age-dependant Dentinal and Pulpal Changes – Structural, Physico-Chemical and Molecular-Biological characteristics"**

### 1. General presentation of the DSc procedure

On the basis of order No P-987/22.06.2021 by the Rector of the Medical University – Plovdiv, I have been selected as a member of the scientific jury for the procedure for acquisition the scientific degree "Doctor of Sciences". The presented set of materials is in accordance with the requirements of the Law on Development of Academic Staff in the Republic of Bulgaria and its Implementing Regulations, as well as the criteria of the Medical University – Plovdiv for the acquisition of the scientific degree. The author has applied 8 scientific publications related to the dissertation.

### Short biographical data for the candidate

Prof. Neshka Manchorova was born in 06.06.1977. In 2000, she graduated with a Master's degree in dental medicine, Faculty of Dental Medicine, Medical University – Plovdiv. In the period 2002-2005, she specialized "Operative Dentistry and Endodontics", and in 2009 acquired the Educational and Scientific Degree "Doctor" in the Department of Operative Dentistry and Endodontics. She holds successive positions of "Assistant" (2002-2009), "Chief Assistant" (2009-2011), "Associate Professor" (2012-2016) and "Professor" (since 2016) in the Faculty of Dental Medicine of MU-Plovdiv, a testament to her rapid career and scientific growth. Prof. Manchorova

participated in a number of training courses and presented results at conferences in Bulgaria, EU countries and USA.

## **2. Relevance of the topic and expediency of the assigned tasks**

The theme of the dissertation work is current and significant: the refinement and explanation of cellular and molecular changes in dental pulp and odontoblasts, which are associated with the initialization of apoptosis, hypoxia, oxidation, autophagy, as well as their regulatory mechanisms, and are a challenge for specialists in the field of dentin and pulp biology. The main directions in the proposed dissertation work are related to consideration of age-dependant changes in dentin and pulp odontoblasts at morphological, structural, physico-chemical and molecular-biological level. The DSc candidate offers and justifies two mechanisms for dentinogenesis without the function of secretory odontoblasts: serum-mediated and apoptosis-related dentinogenesis. The processes of the formation of dentin without the secretory function of odontoblastic cells are poorly studied and unclear. *What is the mechanism, signal transduction and control on apoptosis of pulp odontoblasts and what are the age-dependant features of the process in order to participate in the formation of physiological transparent intratubular dentin are questions that are answered in this work.*

## **3. Knowledge of the problem**

The author of the dissertation knows the problem in details by making an impressive literary overview from 881 sources, of which 9 in Cyrillic and 872 in Latin. She also demonstrates a very good knowledge of the possibilities of a number of modern physico-chemical methods, which motivatedly and successfully are used to meet the objectives set.

## **4. Methodology of the study**

The author presented in an informative way the design of the study on page 11 in the Thesis Synopsis. To solve the main tasks set out in the dissertation objects of the study are selected in 3 age groups and a combination of appropriate physico-chemical and molecular-biological methods are used:

-To determine the morphology and ultrastructural characteristic of dentin and assess changes in physiological ageing, a combination of microscopic techniques is used: light microscopy with polarization microscope, light microscopy of paraffin sections, scanning electron microscopy;

- For phase identification of dentin in different ages and determination of the nano-size of crystallites: X-ray phase analysis is applied;

- To determine the thermal behavior of dentin associated with a complex assessment of changes in its composition in thermal treatment - DTA-TG in combination with gas phase analysis (mass spectrometry) is done;

- To assess the inorganic, organic phase and water in the age-changing dentin: the possibilities of infrared spectrometry with full internal reflection and Raman spectroscopy are used;

- To detect changes in the nanomechanical characteristic of dentin with age: a nanoindentation and atomic-force microscopy are applied;

- To establish age-dependent changes in tissue distribution and cell expression of non-collagen proteins of the SIBLINGs family; to study the mechanisms for apoptosis of odontoblasts in cellular aging and its regulation; to establish the relationship between cellular aging and autophagy in odontoblasts; to establish the correlations between physiological ageing and pulp-dentin homeostasis – immunohistochemistry of paraffin tissue cuts of dentin and dental pulp is applied.

## **5. Characteristics and evaluation of the dissertation work and contributions**

Thesis contains 321 pages, it is illustrated with 40 tables, 30 diagrams and 177 figures.

The one-page introduction is specific and well worded. The abbreviations used followed, making it easier to read the dissertation. The literary review covers 73 pages and is a comprehensive analysis of the currently known new data on the structure and age-dependant changes in dentin and odontoblastic cells at morphological, biochemical and molecular-biological level. The description of the methods of examination is intended to characterise such modern methods and their purpose, that their application becomes pre-justified. Based on a summary of the data from the literary sources, unresolved problems and scientific hypothesis have been identified. The objective is clearly formulated by also having 5 sub-objectives with specific tasks attached to them: Sub-objective 1 – 5 tasks, Sub-objective 2 – 2 tasks, Sub-objective 3 – 2 tasks, Sub-objective 4 – 1 task, Sub-objective 5 – 3 tasks. The accomplishment of each task consists of the components "Material and Methods", "Results and Discussion" and "Conclusion", which makes this part of the dissertation very well structured and shaped within 173 pages. I am particularly impressed by the rich graphic and SEM material, the statistical processing, the precise analytical discussion and



summary of the results. All the facts presented obtained through a variety of research methods confirm that in aged dentin, changes occur in the mineral phase, collagen, bind and free water components. In a special section in the dissertation, the specified scientific hypothesis is summarized and substantiated by derived author original hypothesis of cellular-non-secretory formation of transparent intratubular dentin by serum-mediated and apoptosis-related dentinogenesis. Eighteen (18) specific conclusions are formulated based on the huge material presented. I accept the contributions formulated as objectively reflecting the results presented.

#### **6. Assessment of publications related to the dissertation work**

In connection with the dissertation work Prof. Manchorova offers 8 publications, four of which are in editions, referenced and indexed in the world databases, two of them with IF. The other four publications are in unreferenced journals with scientific review. In two of the works, she is a single author. This fully meets the criteria and requirements of the Law on Development of Academic Staff in the Republic of Bulgaria and its Implementing Regulations, as well as the criteria of the Medical University – Plovdiv. The number of citations referred to also meets the required criteria.

#### **7. Personal participation of the DSc candidate**

My personal impressions are that Prof. Manchorova has amazing skills to bring together a team of scientists working in the field of crystallography, physico-chemistry and molecular biology. In the presented work special attention is paid to all specialists who contributed to the implementation of laboratory tests. The contributions of Prof. Manchorova in the realization of this interdisciplinary dissertation work are indisherable as the initiator of ideas, analyzing and interpreting the results.

#### **8. Thesis Synopsis**

The submitted Thesis Synopsis follows the chronology and approach of the presentation in the dissertation work within 96 pages, containing 9 tables, 21 diagrams and 55 figures. The Thesis Synopsis has been finalized with the contributions of the dissertation work and in addition to the publications related to the theme of the dissertation, 6 more scientific communications from prestigious international scientific forums are mentioned. Thus, the proposed Thesis Synopsis fully meets the requirements of MU.

#### **9. Critical remarks and recommendations**

The thesis presented is very well structured and precisely written. I have a small note concerning the methodological description of the thermal method, which includes DTA-TG and

gas phase analysis by mass spectrometry, in this case a gas-chromatographic method specified by the author is not applied. I have no critical comments and disagreements on the selection of methods, the analysis of the results and their discussion.

### **CONCLUSION**

The dissertation work contains scientific and applied results with original contributions to dental medicine. The requirements of the Law on Development of Academic Staff in the Republic of Bulgaria and its Implementing Regulations, as well as the criteria of the Regulation of Medical University – Plovdiv for the acquisition of the scientific degree are met.

Due to the above, I am confidently giving my positive assessment of the proposed dissertation work and author's Thesis Synopsis and propose to the honorable scientific jury to award the scientific degree "Doctor of Sciences" to **Prof. Dr. Neshka Atanasova Manchorova-Veleva** in professional field: 7.2. Dental medicine, scientific specialty: Therapeutic dental medicine.

23.08.2021 г.

Produced the statment:



N. Petrova