REVIEW

IN A COMPETITION FOR AWARDING AN ACADEMIC DOCTOR OF SCIENCE

IN MU-PLOVDIV

From Prof. Krassimira Todorova-Hayrabedyan, ~~Ph.D, DSc~~
Head of Laboratory for Reproductive OMICs Technologies,
Institute of Biology and Immunology of Reproduction, BAS

Subject: Dissertation for the degree of "Doctor of Science" by Prof. Neshka Manchorova on "Age-dependent changes in dentin and dental pulp - structural, physico-chemical and molecular-biological characteristics"

The materials presented in the competition are well arranged and reflect the requirements of the Law and the Regulations for application of the law for the development of the academic staff in the Republic of Bulgaria, as the materials are presented both on paper and electronically.

Biographical information of the candidate:

Dr. Neshka Manchorova graduated from the Faculty of Dental Medicine at the Medical University, Plovdiv in 2000. In the same year she began to practice in the specialty. From 2002 to 2011 holds the academic position of "assistant" at the Medical University - Plovdiv; In 2009 Dr. Manchorova defended PhD degree - "Doctor" at the same faculty. In 2012 she held the academic position of "Associate Professor". In 2016, Dr. Neshka Manchorova received the academic title of "Professor". During the years of her career development she has attended many courses in the country and abroad, made specializations and participated in many forums and congresses.

Relevance of the topic and significant achievements for science:

The dissertation presented to me for review concerns research on dentin and dental pulp disorders that are caused by age-related changes. Structural, physico-chemical and molecular-biological characteristics have been made. The topic of the research is relevant, as concerns an important, socially significant problem. In the perspective of oral health, human longevity requires the preservation of dental structures. With aging, the dentin becomes harder, but inelastic and brittle, which leads to an increased risk of fractures. The dissertation is original due to the fact that new mechanisms are sought based on the biological basis of age - the dependent changes in odontoblasts and dentinal apposition throughout the life cycle of the organism, which in turn would create a foundation for both therapy and prevention of teeth according to their age, as well as for adequate precautions against cellular aging and degeneration. A panel of molecules that are key to vital processes in the body, such as apoptosis, cell aging, autophagy, has been studied. The development of new biomarkers and tools, as well as the understanding of the key steps and pathways for the development of the disease will be an important step for experimental medicine and translational research.
The main results achieved in this work are related to the detection of CD34 + cells in all age groups, which supports the concept of permanent angiogenesis in the body of the adult, probably for adaptive reasons. Cellular aging has been shown to express more BID and Caspasa-8 than odontoblasts. The results for the distribution of BID and Caspasa-8 in masticatory and frontal teeth show a statistically significant higher expression of both markers in frontal teeth. Statistically significantly more BID and Caspase 8 were found in dental pulp odontoblasts in samples of old pulp, thus protecting the notion that the BID-Caspase-8 signaling pathway has age-dependent activity. There is also a statistically significantly higher immunoreactivity for frontal teeth for JAK1 and STAT3. Immunohistochemically, statistically significant increased expression of COX2 associated with cellular aging of dental pulp was found.

Characteristics of the dissertation and the abstract

The dissertation is written on 321 pages. The structure of the present dissertation includes: Title page, Introduction, Abbreviations, Literary review, Unresolved problems, Scientific hypothesis, Objective, Sub-objectives, each sub-objective includes a different number of Tasks, Materials and methods, Results and Discussion, and Conclusions, which are structured after each sub-goal, Summary and argumentation of the scientific hypothesis, Conclusions and Bibliography. The structure of the dissertation presented in this way is unconventional, but it

is probably written in this way for the convenience of the reader, as the dissertation is interdisciplinary, with diverse methods and thus the research is divided. The literature review is 72 pages long; It is extremely detailed and very illustrative, reflecting both basic and new, modern research in biology and medicine. The Literary Review raises many questions to which there is still no unambiguous answer, with which the author of this paper emphasizes that despite the many studies in the field, many problems still remain unresolved. These questions are a smooth transition to the later hypothesis in the dissertation.

The Materials and Methods sections are described in detail. A significant number of patients (teeth) are represented. In methodological terms, the dissertation is rich, with methods from cell, molecular biology and immunology. All immunological and molecular biological methods used are described in detail, which, if necessary, would facilitate each in the process of repetition. The results and discussions to them are formed in general chapters, which in dissertation work is a modern trend and allows optimized presentation of experimental data and their own hypotheses and analyzes. Precisely arranged microphotographs of very high quality are observed. The results are presented in many figures, tables and diagrams, quite sufficient for such work. For the convenience of the reader, conclusions are written after each result. From the obtained results 18 conclusions were generated in a separate section. The bibliographic reference includes a huge number of sources - 881, including Bulgarian and foreign authors. Numerous contemporary literature sources are cited, which shows the relevance of the information.

The abstract is made according to the requirements and corresponds to the content of the dissertation. It is written on 96 pages, including the chapter "Contributions". A list of publications and participations in congresses is presented.

Scientometric indicators:

1. By group of indicators "A" - 1. Successfully defended dissertation for PhD degree (50 points out of the required 50 points)
2. By group of indicators "B" - Dissertation for the "Doctor of Sciences" (100 points out of the required 100 points)
3. By group of indicators "D" - Scientific publications (139 points out of the required 100 points)
4. By group of indicators "E" - Cited (105 points out of the required 100 points)

The candidacy of Prof. Neshka Manchorova meets the set minimum required points according to the regulations for application of Law for the Development of the Academic Staff in the Republic of Bulgaria (2010) for the scientific degree "DSc" in the professional field 7.1. Medicine, 7.2. Dentistry, 7.3. Pharmacy.

Conclusion:

The dissertation contains scientific and applied results, which represent an original contribution to science and meet all the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria. The presented work is of great interest as a topic and reflects the search for molecular-biological approaches to establish mechanisms for dealing with this socially significant problem.

The dissertation is formed at a good level, is filled with many methods and makes an attempt for a wide-ranging analysis of the problem, raising a number of questions, that is why my personal opinion is that this is a valuable and worthy candidacy for "Doctor of Science ". Due to the above, I confidently give my positive assessment and vote "Yes" the award of the scientific degree "Doctor of Science" to Prof. Neshka Manchorova.

Reviewer:
Prof. Krassimira Todorova-Hayrabedyan, Ph.D, DSc

24.08.2021
Sofia