

Professional opinion

From Assoc. Prof. George Vassilev Hadjidekov, DM

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„St. Kliment Ohridski“

of the dissertation entitled:

„Contrast-enhanced magnetic resonance techniques of pathologies, based on cellular redox-imbalance“, authored by **Dessislava Anri Lazarova**,

for the acquisition of the university and research degree “Doctor” (Doctor of Philosophy) in
the Professional Field

4.1 Physical Sciences – Biophysics,

Higher Education 4. Natural Sciences, Mathematics and Informatics

1. Personal details of the author

Assistant professor Dessislava Anri Lazarova obtained a Master's degree in Molecular Biology - Biophysics at the Faculty of Biology, Sofia University "St. Kliment Ohridski "in 2006. Since 2008 she is a lecturer in biophysics at the Department of Physics, Biophysics and Radiology of the Medical Faculty of Sofia University. From our work in the Department I have direct impressions and excellent appreciation for her professional and teaching skills.

2. Structure of the dissertation

The text of dissertation is structured in the usual format: Review of Literature, Objective and Tasks, Materials and Methods, Results and Discussion, Bibliography in a total volume of 95 Pages. It is illustrated with 39 figures and 1 table. The volume of the individual sections is well balanced, with the largest section "Results and Discussion", which includes 26 figures. The style is very comprehensible, in literary Bulgarian language. The presented autoreferate in a volume of 47 pages corresponds to the content of the dissertation and provides clear and detailed information about the experimental work and the results of the research.

3. Actuality of the topic and relevance of purpose and tasks

The present dissertation thesis of Desislava Anri Lazarova is dedicated to an extremely actual and modern topic in the field of biophysics and experimental imaging diagnostics - development of contrast-enhanced magnetic resonance methods and approaches for visualization of pathologies related to cellular redox status disorders. The methods are based on suitable redox sensors based primarily on nitroxide derivatives, as well as high sensitivity techniques such as magnetic resonance imaging (MRI) and electronic paramagnetic resonance imaging (EPR). The purpose of the study is precisely formulated and directly postulates the connection with the practical applications. The topic of the dissertation is very relevant and interesting in three aspects: (a) from practical point of view, as well as for diagnostic purposes, also for predicting the effectiveness of therapy on diseases, accompanied by a disturbance of the redox signaling, resp. the cellular redox-status of isolated cells, tissues and body fluids – carcinogenesis, neurodegenerative and autoimmune diseases, atherosclerosis, inflammatory processes, etc.; (b) lower toxicity of nitroxides compared to gadolinium complexes (which in our days are widely used in clinical practice) making them attractive and promising as future contrast agents for MRI; (c) expanding the possibilities of applying EPR methods in preclinical diagnostic practice and work-up.

4. Literature review of the topic

The literary review is detailed, balanced and well structured, reflects the current state of the problems studied and is attested that the author knows excellent exposure to the dissertation themes. 144 literary sources has been cited, the majority of them have been published since 2010.

5. Characterization and evaluation of dissertation work

Assistant professor Lazarova has used a wide range of modern methods, which are described in details - 8 preparatory and 10 analytical methods. She has had the opportunity and a rare chance of working on a unique device - 7T MRI unit for small animals, as well as one of the latest EPR spectrometers. Experimental studies were conducted at the National Institute for Radiological Research of Japan (NIRS), Chiba, Japan, conducted on both phantoms and experimental animals under anesthesia. In this context, the majority of the experimental results obtained are of high originality. Two experimental models of animal

pathologies (renal dysfunction and parkinsonism), several experimental models of cultured cells (normal and cancerous with a different proliferative index and the same origin) and several cell-free modeling phantom systems were used in the course of the work.

The obtained results express with an original and confirmatory character. Impressions on the topic of the dissertation thesis has been published in 4 papers with impact factor and 2 in non-impact factor medical and experimental reviews. The total impact factor of the dissertation's publications is 8,904. 73 citations of the articles on the subject of the dissertation project are discovered till the date of the current opinion. The PhD student presented results on the topic of dissertation work at 4 scientific forums.

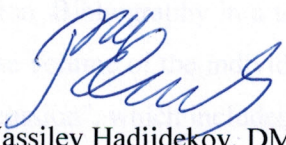
The theoretical and experimental data presented by the applicant fully cover the minimum national requirements for the acquisition of the "Doctor" degree in the professional field 4.1 Physical Sciences, in accordance with the changes in the LDASRB (Law on the Development of Academic Staff in the Republic of Bulgaria) of July 2018 and exceed the minimum requirements, according to the amendments adopted in the Regulations for the Application of LDASRB for the same professional field from 19 February 2019.

6. Conclusion

In summary, the theoretical and experimental developments in the dissertation are very logically planned and realized. Significant results have been obtained, characterized by a high degree of originality and concrete application. The publishing activity corresponds to the national minimum requirements for acquisition of the "Doctor" degree according to art. 1a, para. 1 of the Regulations for the Implementation of the Law on the Development of the Academic Staff in the Republic of Bulgaria. As a result of the above, I strongly recommend the Honorable Scientific Jury for awarding the educational and scientific degree "Doctor" in the professional field 4.1 Physical Sciences, specialty "Biophysics" to Desislava Anri Lazarova.

24 march 2019

Sofia


/Assoc. Prof. George Vassilev Hadjidekov, DM/