

STATEMENT

by Assoc. Prof. Dr. Tamara Ivanova Pajpanova, Institute of Molecular Biology "Acad. Rumen Tsanev ", Bulgarian Academy of Sciences,

on: dissertation for obtaining the educational and scientific degree "doctor",

Dissertation Thesis: "CONTRAST-AMPLIFIED MAGNETIC-RESONANCE TECHNIQUES FOR VISUALIZATION OF PATHOLOGIES RELATED TO BREAKDOWN IN THE CELL REDOX-STATUS",

Author: Desislava Anri Lazarova – PhD student of Independent Education at the Department of condensed matter physics, Faculty of Physics, Sofia University "St. Kliment Ohridski ", Sofia.

General presentation of the procedure

The set of documents provided by Desislava Lazarova includes prepared materials and documents, as well as their electronic form, responding to requirements of the doctoral degree procedure, in accordance with the Law on the Development of the Academic Staff of the Republic of Bulgaria and the Regulations for its application and internal criteria of Faculty of physics, Sofia University "St. Kliment Ohridski ", Sofia.

Actuality and relevance of scientific problems covered by the doctoral thesis

The work presented by Desislava Lazarova concerns the development of contrast-enhanced magnetic resonance methods for visualizing pathologies associated with cellular redox status disorders. Redox imaging is one of the newest and most promising approaches in experimental imaging diagnostics, allowing the nitrox-enhanced MRI to expand the functional imaging capabilities.

The topic is up to date and interesting with the practical applicability both for diagnostic purposes and for the therapy of diseases associated with a redox signaling disorder, redox status of cells, tissues and body fluids.

Dissertation Analysis

The Desislava Lazarova's dissertation covers 95 pages, including 1 table, 39 figures and cited literature (144 sources in total). The dissertation is structured according to the generally accepted rules.

The Literary Review

The introduction accurately reflects the essence of the study. The overview (pages 2-31) is clearly arranged, written in a concise and logical manner, which is a proof of a very good knowledge of the literature. The problems in the given field and the possibilities for their solution have been defined and on this basis a smooth transition has been made to the formulation of the goals and tasks of the dissertation.

The aim of the dissertation thesis is clearly expressed, and four tasks have been formulated for its implementation.

The Materials and Methods section (pages 33-46) covers the materials used by the PhD student as well as the methods by which it serves to perform the experimental tasks. The methods are advanced, and some of them are very innovative, described in a sufficiently detailed and understandable way, allowing for reproduction if necessary.

In the section "**Results and Discussion**" (pages 47-85), Dr. Lazarova analyzed in detail the data obtained by her in the elaboration of procedures for the application of nitrox-enhanced EPR to visualize and evaluate the cellular redox status of isolated cell lines *in vitro*; of the tissue redox status in mice with an experimental model of hypercholesterolemia using MRI and mito-TEMPO as the contrast substance and the tissue redox status in the cortex and dopaminergic region in the brain of mice with an experimental model of parkinsonism using MRI and nitroxides as contrast media.

From the formulation of the goals and objectives of the dissertation as well as and the description of the experimental results, it can be seen that the studies were planned very carefully and thoughtfully and carried out with high precision - with all necessary controls. It is noteworthy that somewhere in the description of the results, the Ph.D. student has also inserted a brief discussion to justify the approach selected for each subsequent stage of the research.

In the last pages of the dissertation, Desislava Lazarova formulates **Conclusions** (pp. 177-178) and **Contributions** (page 179). She outputs **8** conclusions that reflect the main results of the thesis. They were described sufficiently concise and informative. The conclusions show that the goal and objectives are fulfilled.

Overall, the work is characterized by a high degree of originality, innovativeness and practical applicability.

The contributions of the dissertation work have a markedly applied character: a new methodical approach was developed using EPR to identify isolated cultured cell lines of the same origin but different proliferative activity; a new methodical approach has been developed for the early diagnosis of renal damage *in vivo*, based on changes in tissue redox status.

Lazarova discloses the possibility of using mito-TEMPO as a new contrast agent for early diagnosis of renal damage by nitrox-enhanced urography.

The results included in the dissertation of Desislava Lazarova were published in six scientific reports. Four of the articles are in reputable scientific journals with a general impact factor of 8.904 - *ACS Chem. Neurosci.*; *Adv. Clin. Exper. Med.*; *Gen. Physiol. &*

Biophys. Two of the papers are review articles in Bulgarian journals (*Trakia J. Sci.*) And (*Un., St. Kliment Ohridski*). Desislava Lazarova is the first author in two of the publications. There were 73 citations, of publications related to the dissertation topic.

Correspondence between the autoreferate and the dissertation

Desislava Lazarova presented an autoreferate, written according to the requirements. The latter adequately and sufficiently fully reflects the structure, content and conclusions of the dissertation.

All that has been said here gives me the opportunity to emphasize that the presented work fully meets the requirements of a thesis on the acquisition of the Doctor's educational and scientific degree.

That is why I give a positive assessment and I suggest to the honorable members of the Scientific Jury to vote for the award of this degree to **DESISLAVA ANRI LAZAROVA**.

21.03.2019

Dr. Tamara Pajpanova