OPINION

by Prof. Dr. Balik Malomirov Dzhambazov

of a dissertation for the award of the scientific degree **"Doctor of Sciences"** (DSc)

in the field of higher education 4. Natural Sciences, Mathematics and Informatics

professional field 4.3. Biological sciences; scientific specialty **Molecular Biology**

Candidate: *Chief Assistant Professor Dr. Tihomir Iliev Vachev*

Title: «**Comparative genomic, transcriptomic and proteomic studies in neurodevelopmental disorders**»

1. General presentation of the procedure and the candidate

The set of digital materials presented by Dr. Tihomir Vachev on CD is in accordance with Article 45 (4) of the Regulations for development of the academic staff of PU. In connection with the defense of the dissertation, a total of 9 publications were presented, 3 of which were reviews. The candidate is a leading author in 5 of the publications. The presented scientific activities cover the minimum national requirements for the individual groups of indicators for obtaining the scientific degree "Doctor of Science" in a professional field. 4.3. Biological Sciences.

Ch. Ass. Prof. Dr. Tihomir Vachev has completed his bachelor's and master's degrees at the University of Plovdiv "Paisii Hilendarski", after which in 2012 he defended his PhD degree in "Molecular Biology" at the University of Plovdiv "Paisii Hilendarski". After showing scientific interests in psychiatric diseases, in 2016 Tihomir Vachen defended his second PhD degree in "Genetics" at the Medical University – Plovdiv. The title of his PhD thesis was "Analysis of the expression profile of noncoding miRNA genes in patients with schizophrenia through large-scale miRNA microarray analysis and quantitative high specific RT-PCR".

The present dissertation is a kind of continuation of his scientific interest in this field.

2. Actuality of the subject

The persistent trend reported in recent years to increase the incidence of mental disorders determines the topic of the dissertation as relevant, moreover, that scientific advances in this field are not many and still there is a need of methods, tools and criteria for clear classification and distinction of different types of mental disorders. The search for specific biomarkers is a key moment in the development of clinical diagnosis and therapy of this type of disease. In this direction is the present dissertation of Dr. Tihomir Vachev.

3. Comprehension of the problem

The extensive literature review on the different types of mental disorders, the factors that influence the development of these diseases, as well as the search for a genetic link, show that the candidate is not only well aware of achievements in this field, but also aware of unresolved issues and guidelines for future research.

4. Research methodology

In the present dissertation an integrative approach is applied, which combines genomic, transcriptomic and proteomic methods of analysis in order to obtain a complete picture of the causes of autism spectrum disorders, the mechanisms of their development and the possibility of influencing specific symptoms. The large amount of data obtained by these methods requires time and specific software products for their complex analysis and conclusions, which determines the slower progress in this field of science.

5. Characteristics and evaluation of the dissertation and the contributions

The presented dissertation can be significantly optimized. The literature review contains a lot of unnecessary information that has nothing to do with the topic of the dissertation. Many of the literature sources are incorrectly cited. The inclusion of information and results for both schizophrenia in adults (which are a continuation of research on patients from the previous dissertation) and for autism spectrum disorders in children creates confusion for the overall vision. There is no a separate section where the goals and tasks of the dissertation are formulated. At the beginning of the section "Results" there are 2 goals of the research, which do not cover the content of the dissertation. The "Materials and Methods" section is unnecessarily detailed. It is not necessary to present the protocols for working with the individual kits. On the other hand, it is not clear how proteins are isolated? The lack of formulated specific goals and objectives of the dissertation makes it difficult to fully analyze and evaluate the large volume of results presented in the relevant section. Working with this type of data requires not to present all the results obtained, but to select those that have an important role and significance for the research topic and support the hypothesis. The discussion is relatively well structured, but there is not always a direct link between the results obtained and the data discussed by other authors. It is not clear whether the figures used in the discussion have been authorized, as they are under copyright protection (Kanehisa Laboratories). There is a general conclusion, but there are no clearly formulated scientific conclusions. The list of literature sources is presented in a different style, with many of the literature sources being duplicated.

Despite the stated disadvantages, the dissertation unequivocally contains scientific and fundamental contributions, namely the identification of candidate miRNA molecules, protein-encoding genes and proteins with potential characteristics of biomarkers in the mental disorders, as well as applied contributions - use of DNA bank of patients for future studies.

I do not accept the mentioned scientific-methodological contributions, since there are not methodologies developed and proposed by the candidate, but widely used applied methods of analysis.

6. Evaluation of the publications and the personal contribution of the candidate

In connection with the dissertation, 9 scientific articles are presented in English in international peer-reviewed journals, 3 of which are reviews. Dr. Tihomir Vachev is a leading author in 5 of the publications, which unequivocally shows his contribution and merits for the results obtained. The scientific metrics fully cover the requirements of the Regulation for the development of the academic staff in the Republic of Bulgaria, the Regulation for its implementation, the Regulation for the development of the academic staff of PU and the Criteria of the Faculty of Biology regarding the award of the scientific degree "Doctor of Sciences".

7. Summary of the candidate's contributions

The summary adequately reflects the results of the dissertation. The individual sections of the dissertation are presented correctly, but the authors whose results are cited and discussed have been removed from the "Discussion" section, which would not give the necessary information to the readers who have only the author's summary. There is a "Goals and Tasks" section here, but again no "Scientific conclusions".

8. Recommendations for future use of dissertation contributions and results

My recommendations to Dr. Tihomir Vachev is to pay more attention to the details and the terminology used. The obtained results should be used for validation and validation of specific biomarkers for diagnosis of the studied mental disorders.

CONCLUSION

The dissertation contains scientific and applied results, which represent an original contribution to science and meet the requirements of the Regulation for development of the academic staff in the Republic of Bulgaria (RDASRB), the Regulation for application of RDASRB and the relevant Regulation of PU "Paisii Hilendarski". The presented materials and dissertation results correspond to the specific requirements of the Faculty of Biology, adopted in connection with the Regulation of the University of Plovdiv for application of RDASRB.

The dissertation shows that Dr. Tihomir Vachev has in-depth theoretical knowledge and professional skills in the scientific specialty Molecular Biology, demonstrating qualities and skills for conducting research with original and significant scientific contributions.

Due to the above, I give my positive assessment of the research presented in the dissertation, summary, results and contributions, and I propose to the esteemed scientific jury to award the scientific degree "Doctor of Science" to Chief Assistant Professor Dr. Tihomir Vachev in the field of higher education: 4. Natural Sciences, Mathematics and Informatics, professional field 4.3. Biological Sciences (Molecular Biology).

08.02.2021   **Prepared the opinion**: ....

Prof. Dr. Balik Dzhambazov