#### **REVIEW**

About the competition for "Associate Professor" in professional management 4.3. "Biological Sciences", specialty "Cell Biology", announced in SJ no. 21 of 15.03.2022 for the needs of cat. "Cell Biology and Biology of Economics" at the Faculty of Biology of Sofia University "St. Kliment Ohridski"

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### 1. Common part

The competition for the academic position "Associate Professor" in Professional Field 4.3. "Biological Sciences", specialty "Cell Biology" was announced in SJ 21 of 15.03.2022 for the needs of cat. "Cellular Biology and Biology of the City", Faculty of Biology, Sofia University "St. Kliment Ohridski". The only candidate in this competition is Ch. Assistant Professor Dr. Georgi Nikolaev Georgiev, working lecturer on the basis of the employment contract at to the same department. The review of the documents shows that the competition procedure has been followed, as well as that the documents have been prepared in accordance with the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria and the Regulations for its implementation.

# 2. Biographical data about the candidate

In 2007, Ch. Assistant Professor Dr. Georgi Nikolaev Georgiev graduated from the Faculty of Biology at Sofia University "St. Kliment Ohridski "as a Master in Cell Biology and Pathology. His professional career dates back to the beginning of 2005, when he started working as a biologist-specialist, and in the period 2007-2014 he held the academic positions of assistant and head, assistant at IBIR, BAS. In 2014 he started working as Ch. assistant in cat. "Cell Biology and Developmental Biology" at the Faculty of Biology, Sofia University, where he still works

today. Since 2012 he has been an ONS doctor of science in Animal and Human Physiology, awarded for his dissertation on "The role of melatonin and growth factors in the paracrine regulation of steroidogenesis and functional characteristics of human reproductive cells." The case that ch. Assistant Professor Dr. Georgi Georgiev has spent the necessary time in each of the above academic positions, which ensures the approval of specific duties and responsibilities, according to the cost of their job descriptions. He also has administrative experience, which is based on his participation as a member of the Faculty Quality Committee and the Election Commission.

#### 3. Scientific works

# 3. 1. Overview of scientific papers and their citation

With his doctoral dissertation in 2007, Ch. Assistant Professor Dr. Georgi Georgiev satisfies indicator A. The total number of published works of Ch. Assistant Professor Dr. Georgi Georgiev for this competition is 17. The required 100 points for indicator B are covered by five publications in scientific journals, which according to the criterion quartiles (Q) are divided as follows: Q1 - 2, Q2 - 2, Q3 - 1, all of them with IF and gaining a total of 105 points. According to indicator D, 12 scientific publications are presented, of which 10 are in journals with impakt faktor (IF) and one with SJR. They provide 250 points due to the distribution Q1 - 4, Q2 - 6, Q3 - 1 and one chapter of a book in English. In six of them Ch. Assistant Professor Dr. Georgi Georgiev is the first author, in one - the second, and in three - the last, which testifies to his very active participation in their production and writing. Most publications are in high ranking scientific journals such as the Journal of Reproductive Immunlogy, the International Journal of Molecular Sciences, Chemico-Biological Interactions, the World Journal of Gastroenterology, Membranes and others.

Indicator D presents 28 citations found in the databases of Scopus and ISI Web of Science, and 5 others. The total number of citations published in the Scopus system as of 26.05.2022 is 25. Scopus h-index = 3, but it is difficult to account because the candidate in this competition has published under different surnames due to the wide distribution of his surname.

Ch. Assistant Professor Dr. Georgi Georgiev has participated with a poster or report in seven international and national scientific conferences.

These scientometric indicators exceed the minimum requirements for the academic position of "Associate Professor" according to the Regulations for the implementation of the

Academic Staff Development Act of the Republic of Bulgaria and the Regulations on the conditions for obtaining scientific degrees and holding academic positions at Sofia University. The research and works of Ch. Assistant Professor Dr. Georgi Georgiev, as well as his contributions are on the topic of the competition.

## 3.2. Evaluation of the scientific contributions of Ch. Assistant Professor Dr. Georgi Georgiev

Ch. Assistant Professor Dr. Georgi Georgiev has arranged the scientific and scientific-applied contributions to this competition in three groups: 1) contributions related to immunoendocrine and paracrine interactions in the regulation of steroidogenesis, cell cycle and differentiation; 2) contributions related to the mechanisms of action of antitumor and anti-inflammatory agents with therapeutic action and 3) contributions related to the mechanisms of regulation of cell rest and proliferation. All contributions are in the professional field of this competition and are formulated in detail.

Everywhere I have united the contributions of a fundamental and scientific-applied nature. The reason for this is that for some of them, such as contributions I.1.1., II.1.2., I.1.3, II.1.1. II.1.2 and III.1.1. according to the original numbering, it is difficult to judge whether they are only scientific, because in the field of research of the candidate in this competition, a fundamental contribution can easily acquire an applied character. This is because the data on the intracellular signaling chains of the studied mediators - the hormone melatonin, the cytokines leukemia/leukocyte inhibitor factor (LIF) and oncostatin M (OSM), and transforming growth factor beta (TGF- $\beta$ ) allow to act with pharmacological agents on these metabolic pathways to achieve therapeutic effects. I accept the thematic division of the contributions from Ch. Assistant Professor Dr. Georgi Georgiev in three groups.

3.2.1. Immunoendocrine and paracrine interactions in the regulation of steroidogenesis, cell cycle and differentiation (publications B4.2, B4.3, B4.4, D7.1 and D7.2)

For the first time, in cell cultures of human fibroblasts and primary human granulosa cells, melatonin was found to alter the expression of Yamanaka transcription factors for cell reprogramming and differentiation by a signaling chain involving melatonin receptor 1 (MT1) and ERK1/2 kinase. 2). In the same cells, melatonin increases the expression of P450 aromatase, which confirms its importance for follicle maturation and the secretory phase of the cycle (B4.4). Conversely, in human competent sperm, MT1 reduces or even blocks the expression of P450

aromatase, resulting in significantly higher testosterone /estradiol ratios in healthy donors than in sterile donors (B4.1).

Expression of the FSH receptor and aromatase P450 and estradiol secretion were detected in the COV434 human granulosa cell line. Activation of the signaling pathway by Janus kinases/STAT proteins (JAK/STAT) in human granulosa cells from LIF and OSM has been shown for the first time (D7.1., D7.2).

Melatonin-dependent cell cycle regulation and proliferation in phytohaemagglutininstimulated human peripheral blood mononuclear cells (PBMCs) have been studied, showing the expression of both melatonin receptors (MT1 and MT2) in PBMC for the first time. Through them, melatonin retains activated PBMCs in the G0/G1 phase and increases the probability for polyploidyty.

3.2.2. Mechanisms of action of antitumor and anti-inflammatory agents with therapeutic use (publ. G7.4, G7.5 and G7.11)

The effect of co-administration of antitumor agents on human lung adenocarcinoma cell lines has been studied to develop more gentle tumor therapies. The data obtained showed for the first time the additive cytotoxic effect of miltefosine and dimethylsphingosine on these cells, suggesting the possibility of treating lung cancer with reduced doses of cytostatics (D7.4).

Antioxidant effect and changes in the lipid composition of the membrane shelves with resveratrol were found in three-dimensional fibroblast cultures. This stilbenoid increases the content of sphingomyelin and reduces phosphatidylcholine and cholesterol (G7.5). The same model system showed a change in the composition of phospholipids and fatty acids on the plasma membrane when treated with the polyphenol quercetin. It increases the amount of saturated fatty acids and reduces the amount of all polyunsaturated fatty acids in membrane phospholipids. Quercetin also inhibits apoptosis by increasing phosphorylation of protein kinase B (Akt) and Bc1-2 protein expression. (D7.11).

### 3.2.3. Regulation of cell rest and proliferation (publ. G7.3, G7.7 and G7.10)

The involvement of the enzymes superoxide dismutase (SOD) and catalase in the regulation of the transition between rest and proliferative status in human and mouse fibroblasts has been shown. Tenfold increased levels and activity of SOD and catalase proved to be

characteristic markers for retention of the studied fibroblasts in stage G0. The results suggest the involvement of reactive oxygen species with signaling function such as superoxide anion and hydrogen peroxide in maintaining rest at this cell type (D7.3).

It was found that when the cells enter the G0 state, the kinase ERK1/2 is retained in the membrane shelves. This reduces its localization in the nucleus, and hence the process of cell proliferation. The translocation of ERK1/2 and its limited activity in lipid shelves in the G0 stage is considered to be a major factor in inhibiting the proliferation of primary culture from human fibroblasts (G7.7).

In another series of experiments, it was found that high glucose concentrations slow the healing of experimentally injured three-dimensional fibroblast cultures due to reduction of their transdifferentiation into myofibroblasts, which is associated with inactivation of the TGF- $\beta$  signaling. These data could be used to develop a drug to improve wound healing in patients with hyperglycemia.

I have some recommendations for contributing:

- 1. In the first main contribution, to correct the places of publications B4.3 and B4.4, because they have been exchanged.
  - 2. To clarify abbreviations such as PHA, PBMC, COV484, LIF, OSM, JAK-STAT in the text.

In addition, I note that against the background of excellent prepared set of documents, the CV of the candidate in this competition is very concise. It lacks data on participation in scientific societies, scientific and educational projects, degree of proficiency in the indicated German and English languages, etc.

## 3.3. Participation in research projects

Ch. Assistant Professor Dr. Georgi Georgiev has participated as a member in a total of 8 scientific and educational projects. One of them is related to the training of PhD students and young scientists. It is entitled "Fundamental and applied training of doctoral students, postdoctoral students, postgraduates and young scientists in interdisciplinary biological fields and innovative biotechnology" and is funded by the Ministry of Education and Science of Bulgaria and the European Social Fund. Another project is for building and developing scientific infrastructure, four are research projects, one is related to the coordination of research in the field

of personalized medicine through the European infrastructure EATRIS and one - to build and develop capacity in technology for assisted reproduction and regenerative medicine in Republic of Serbia. The diverse experience gained over a decade in the field of project activities supposes the successful participation of Ch. Assistant Professor Georgi Georgiev in future national and international projects, including those under his leadership.

4. Teaching experience and classroom employment of Ch. Assistant Professor Dr. Georgi Georgiev

The teaching experience of Ch. Assistant Professor Dr. Georgi Georgiev is intense and diverse. The report from the last five school years shows the workload invariably above the Sofia University "St. Kliment Ohridski" requirements for classroom and extracurricular employment.

Ch. Assistant Professor Dr. Georgi Georgiev is the holder of the mandatory courses for bachelor's students in Cytology, specialty Biotechnology and Ecology, part-time study, Animal Cell Cultures and Hybridoma Techniques for students in Biotechnology, full-time training in Cytology, Histology and Embryology for students in binary pedagogical specialties. In addition, he leads the courses in Cell Signaling, Signal Pathways in the Cell and Modern Methods in Cell Biology for masters in the master's programs of Departmet of Cell Biology and Developmental Biology, which have always been of great interest to students. He also conducts exercises for many of the mentioned courses. Under his scientific supervision for the period 2015-2020, six diploma theses of bachelor's and master's students have been successfully defended.

In 2012 he received a grant from DAAD to work at the Friedrich Schiller University in Jena, Germany.

I know ch. Assistant Professor Dr. Georgi Georgiev for several years. I would characterize him as a responsible, ethical and hardworking teacher with a serious interest in scientific research. I am sure that he will still succeed in teaching and research.

## Conclusion

Scientific creativity, established citations, participation in projects, scientific and scientific-applied contributions, participation in national and international conferences of Ch. Assistant Professor Dr. Georgi Nikolaev Georgiev fully meet the criteria for "Associate Professor" of the Law on Development of the Academic Staff of the Republic of Bulgaria, the

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Rules for implementation of the Law on the Development of the Academic Staff of the Republic of Bulgaria and the Rules on the conditions for obtaining degrees to academic positions at Sofia University "St. Kliment Ohridski". His teaching activity is intensive and is entirely in the field of the competition. All this gives me reason to confidently recommend to the esteemed Scientific Jury to vote FOR the proposal to the Faculty Council of the faculty of Biology for the election of Ch. Assistant Professor Dr. Georgi Nikolaev Georgiev for Associate Professor in Professional Field 4.3. "Biological Sciences", specialty "Cell Biology" for the needs of the Department of "Cell Biology and Developmental Biology" at the Faculty of Biology, Sofia University "St. Kliment Ohridski".

June 21, 2022.

Reviewer:

/ prof. Dr. Hristo Gagov /