

## **REVIEWER REPORT**

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On the evaluation of the candidates in a competition for the full professor position at the Institute of Microbiology "Stefan Angelov" - Bulgarian Academy of Sciences for the needs of the Laboratory of "Experimental Immunology" at the Department of "Immunology". Area of the higher education 4. Natural Sciences, Mathematics, and Informatics; Professional field - 4.3. Biological Sciences (Immunology)

By order № I-82 / 01.07.2020 of the Director of the Institute of Microbiology (IMikB) at BAS, I was appointed as a member of the scientific committee in the above competition, announced in the State Gazette issue 47 / 22.05.2020 and the website of IMikB.

I declare that I do not have a conflict of interest within the meaning of § 1, item 2a, or restrictions for related parties, and within the meaning of § 1, item 5 of the additional provisions of the Academic Staff Development Act in the Republic of Bulgaria. I also declare an absence of joint publications with the candidate for the full professor position.

### **I. General comments**

Only one candidate has submitted documents for participation in the announced competition - Associate Professor Dr. Andrey Ivanov Tchorbanov, Head of the Department of Immunology at the same institute. All necessary documents are presented following the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria (LDASRB) and the Regulations of the Institute of Microbiology Biology - BAS for its implementation.

### **II. Professional and academic development**

Assoc. Prof. Tchorbanov graduated biotechnology at the Faculty of Biology of the Sofia University "St. Kliment Ohridski", with a specialty "Genetic and cell engineering in prokaryotes and eukaryotes". He specialized in immunology at the University of Utrecht, the Netherlands, under the Copernicus program (1996-1997) and at the National University of Taiwan, Taipei

(2003). His professional development is focused in the field of experimental immunology, passing through NCIPD - Section "Applied Immunology and Biotechnology" (1992 - 1998). Since, 1999 he was associated with IMikB - BAS, Section "Immunology" as Assistant professor. In 2002 he defended his doctoral degree on "Engineering and genetically engineered chimeric molecules as antigens". In 2009 he was elected as Associate Professor in Immunology at the same Institute, which he still holds. Assoc. Prof. Tchorbanov has over 29 years of continuous work experience in the specialty of the competition, 11 of which as an associate professor, which covers the requirements for compliance with LDASRB.

### **III. Scientific achievements**

The total scientific output presented by Assoc. Prof. Tchorbanov includes 64 articles in peer-reviewed journals, 33 of which have been selected for participation in this competition. All 33 publications have not been reviewed in previous competitions for awarding scientific degrees or academic positions. He divided this list into three parts and clearly distinguished the articles which meet the criteria for holding the academic position Professor, according to the LDASRB (16). For criteria "B" 5 articles are subject to review - 26, 28, 29, 30, and 31 (4 with Q1 and 1 with Q2). Criteria "D" include articles 32, 33, 35, 37, 42, 46, 48, 49, 55, 56 and 57 (6 with Q1 and 5 with Q2). They are summarized in Table 1. By adding articles 27, 36, 39, 43, 44, 45, 47, 50, 51, 52, 54, 58, 59, 60, 62, 63 and 64, Assoc. Tchorbanov also covers the additional criteria included in the Regulations of IMikB-BAS to have 20 publications, following habilitation in 16 of which to be a leading author. He has 33 publications after habilitation and is a leading author of 23, thus accounting for 70% of his total scientific output.

The scientific indicators were taken from the Thomson Reuters Web of Science database. According to this database, the h-index of the candidate for his entire scientific career is 12.

The citations' column of Table 1 includes citations of all articles. I accept all the above citations because the auto-citations of all co-authors are excluded. Three hundred fifty-four of these citations are in scientific journals, referenced and indexed in world databases Web of Science. Thus, after the calculations made by me on the indicator "D-11", Assoc. Prof. Tchorbanov scored 833 points.

**Table 1.** Candidate's group indicators (A to E) following LDASRB and the Regulations of the Institute of Microbiology Biology – BAS

| Indicator's group   | Indicators number   | Minimum number of points  | Candidate's points |
|---|---|---|--------------------|
| A   | #1 – PhD Degree   | 50  | 50                 |
| B   | #2 – DSc Degree   | -   | -                  |
| C1  | #4 – publications   | 100   | 120                |
| C2  | #7 – publications   | 200   | 250                |
| D   | #11 – citations   | 100   | 833                |
| E   | ##13, 16, 17, 18  | 150   | 465.376            |
| <b>Total</b>  |   | <b>600</b>  | <b>1709.376</b>    |
| <b>Additional criteria</b>                                      |   |   |                    |
| A number of publications in journals with IF, monographs, etc.  | 20 (after "associate professor") in 16 of them leading or the corresponding author) | 33 following habilitation, 23 as a leading author (70%)   |                    |
| Citations * (without autocitations of all authors)              | 400   | 479<br>354 within the Web of Science;<br>125 - in other databases   |                    |
| IF*   | 40  | 141.754   |                    |
| h-factor* (excluding auto-citations) 10                         | 10  | Web of Science – 12   |                    |
| Management of:  | 3 projects  | Head of 13 (2 current);<br>Partner in 24 projects (10 current);<br>Member in 9 (1 current).<br>He participated in the competition with five international ones. |                    |
| Supervisor of:  | 2 successfully defended doctoral student  | Co-supervised -1<br>Supervised - 3  |                    |
| Participation in national and international scientific forums * |   | 315 (82 after habilitation)   |                    |

\* For the whole scientific career

Assoc. Prof. Tchobanov has participated and is actively involved in the development of 46 research projects, leading 13. Their detailed distribution is shown in Table 1. Andrey Tchobanov has extensive experience in leading Bulgarian teams to implement several international projects. Only five projects have been selected for participation in this competition. Three of them are between the Bulgarian Academy of Sciences and the Academies of Sciences (Slovakia, Hungary), or the Italy National Council for Scientific Research. The Pasteur Institute funds the other two. Raised funds for these 2 projects are 103 000 euros (201 880 levs) = 40. 376 points to the criteria "E № 18". I make a critical remark that no evidence (contracts) has been submitted to confirm financial support. According to the indicators from group "E" Assoc. Prof.

Tchorbanov has over 400 points, which is many times higher than the minimum of 150 points required by the LDASRB.

The results of the candidate were presented in 315 scientific communications and reports, 82 after holding the academic position Associate Professor. The conferences' presentations contribute to the great promotion of his scientific output to the international community.

It can be seen (Table 1) that the total number of candidate's points is over 2.5 times higher than the required minimum for the group of indicators from A to E, covering the essential research assets. The impressive impact factor (IF), the number of citations, and popularization of the scientific results (congress activity) make indisputable the candidacy of Assoc. Prof. Tchorbanov for the Full Professor position.

#### **IV. Research activity**

I accept the reference submitted by the applicant for the fulfillment of the requirements according to the LDASRB based on 16 journal articles included in criteria "C". Summarizing it, the scientific contributions of Assoc. Prof. Tchorbanov can be divided into the following 3 important areas:

##### ***A) Development of new DNA and protein-containing engineered vaccines, including new adjuvants.***

The use of engineered and genetically engineered chimeric molecules to target antigens to Fc $\gamma$ -receptors and complement receptors makes it possible to modulate the immune response in a direction desired by the researcher. Assoc. Prof. Tchorbanov achieved this by creating a DNA vaccine encoding antibody fragments specific for activating surface coreceptor cell molecules. The vaccine contains a DNA chimeric molecule that encodes hemagglutinin from influenza A virus, part of the T- and B-cell epitopes. A vaccine containing a variety of DNA constructs encoding single-stranded variable fragments (scFv) of a murine anti-human Fc $\gamma$ RI monoclonal antibody added to the pTriEx-3 Neo vector system has been developed (publ. 15). Experimental protocols have also been developed, allowing the construction of genetic molecules consisting of different light and heavy chains, and carrying other model antigens (publ. 11).

New vaccines are characterized by high safety and lack of side effects, although their disadvantage is the low immunogenicity. Adjuvants are substances that can increase the strength and duration of the immune response, as well as to increase the effectiveness of the vaccine. The Assoc. Prof. Tchorbanov's team researched hemocyanin from *Rapana thomasiana* and *Megathura crenulata* (publ. 6) and proved that its molecule is structurally similar to KLH. Therefore it would have a robust immunostimulatory effect. Immunization of mice with influenza vaccine or tetanus toxoid in combination with hemocyanins from *Rapana thomasiana* (RtH) and Keyhole limpet (KLH) has been shown to induce an anti-influenza cytotoxic response for at least five months, as well as, a humoral response to viral proteins. Similar results were obtained with hemocyanin isolated from the land snail *Helix pomatia* in combination with common antigens (publ. 13).

Hemocyanin has also been studied as an immunostimulant in various cancers. Studies performed with hemocyanins isolated from *Rapana thomasiana* and *Helix pomatia* have shown in vivo anti-tumor and anti-proliferative properties in a mouse model of colon cancer developed by the candidate (publ. 12).

***B) Selective suppression of the pathological response in mouse and human models of autoimmunity (systemic lupus erythematosus and type I diabetes).***

The systemic lupus erythematosus (SLE) is a polygenic autoimmune disease characterized by B-cell hyperactivity, leading to the presence of autoantibodies to nucleoprotein antigens (ANA), the formation of immune complexes, and inflammatory processes in many organs and tissues.

Assoc. Prof. Tchorbanov's main achievements are summarized as follow:

- Clarification of the pathogenesis of SLE. An original experimental model was developed in which human cells from SLE patients were transferred to SCID mice that did not have T- and B-lymphocytes and could accept xenogeneic cells (publ. 2, 8, 9).

- Elucidation of cellular mechanisms of increased expression of surface inhibitory FcγIIB receptors in lymphocytes from lupus mice and healthy mice with IVIg in vitro and in vivo (publ. 1).

- Development of an innovative approach for selective suppression of autoreactive B-lymphocytes by creating chimeric protein molecules consisting of multiple DNA mimotopic peptides linked to rat anti-mouse CD32 (Fc $\gamma$ RIIb) monoclonal antibody (publ. 4).

- Characterizing the effect of chimeric molecules (IgG Fc $\gamma$ RIIb receptor) to specifically suppress autoreactive B- lymphocytes in a pristane-induced autoimmunity model in SCID mice (publ. 3).

- Monitoring the effects of nucleic acids inducing complement activation, leading to masking and removal of apoptotic cells with exposed nuclear components. Binding of complement C3 to various forms of nucleic acids has been shown to target lupus and lead to the development of ANA (publ. 5).

- Chimeric molecules have been developed and studied in detail. These molecules selectively modulate the activity of GAD65-specific B cells in type I diabetes, together with the production of anti-GAD65 IgG autoantibodies by cross-linking inhibitory CD35 with the B-cell receptor (publ. 16).

***C) Newly synthesized cyan dyes and their application as fluorescent markers for analysis of various cellular processes.***

A series of asymmetric monomethine cyanine dyes have been synthesized and characterized in cooperation with various scientific teams. It has been demonstrated that some dyes can stain live macrophages and apoptotic splenocytes and might be used as fluorescent markers for living cells, and apoptosis' analysis (publ. 7, 10, 14).

## **V. Educational, expert activity and awards**

Until the moment of application (2012-2020) Assoc. Prof. Tchorbanov has declared more than 1050 teaching hours in universities and research institutes, for which no evidence has been presented.

He has supervised 4 successfully defended doctoral students (Table 1) and is a co-authored 2 patents.

Assoc. Prof. Tchorbanov has been a member of the BAS's General Assembly since 2020 and a representative of Bulgaria in the Program Committee for Research and Innovation of the

European Union "Horizon 2020" in the Commission "Challenges to the European Bioeconomy: Food Security, Sustainable Agriculture, and forestry, maritime, marine and inland water research "(from 2013 until now). He is chairman of the section "Immunology" at the Union of Scientists in Bulgaria. He is also a member of the international professional, scientific associations - European Federation of Immunological Associations, and European Association for Diabetes Research.

For his scientific achievements, Assoc. Prof. Andrey Tchorbanov has been awarded several national awards: Award of the Stefan Angelov Foundation for the best work of a young microbiologist in Bulgaria - 2000; Awards from competitions of the Union of Scientists in Bulgaria - "Diploma of Excellence" (2011 and 2013). He twice won the most prestigious Bulgarian Pythagorean award in the field of scientific research - for biomedical sciences (2012) and an established scientist in biomedical sciences (2017), as well as an outstanding award of the Kosovo Association in Allergology and Immunology (2017).

## **VI. Conclusion**

I have the pleasure of knowing Assoc. Prof. Andrey Tchorbanov personally and for years witness his success as a researcher and head of the Department of Immunology at IMikB-BAS. He is an established scientist with a clearly defined research profile in the field of immunology, with significant scientific and public authority. Its scientific production meets all formal requirements of LDASRB and the internal conditions of IMikB-BAS for holding the academic position of "Professor".

He covers and, by some indicators, far exceeds the minimum national requirements for holding this position. He has extensive experience in leadership and teamwork, competencies, and skills for concept development and implementation of scientific strategies in the country and abroad. Based on those mentioned above, I recommend the Honorable Scientific Jury to select Assoc. Prof. Andrey Ivanov Tchorbanov as a "Professor" in the professional field 4.3. Biological sciences, scientific specialty "Immunology".

August 28, 2020

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