

# Statement

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*From Assoc. Prof. Dr. Biliana Pancheva Nikolova*

*Institute of Biophysics and Biomedical Engineering, BAS*

*According to a competition for holding an academic position, professor in the scientific field 4.3 Biological Sciences (Biochemistry), announced in SG no. 63 of 30.07.2021 (correction in SG No. 65 of 06.08.2021), announced for the needs of the Medical Faculty.*

With the only candidate submitted documents for participation: Assoc. Prof. Dr. Albena Georgieva Yordanova.

By order of the rector of Sofia University "St. Kliment Ohridski" I have been appointed a member of a scientific jury in the competition described above.

At the first meeting of the scientific jury we got acquainted in detail with the materials provided by Assoc. Prof. Dr. Albena Yordanova and found that they meet the requirements of the law on the development of the academic staff of the Republic of Bulgaria.

Assoc. Prof. Yordanova obtained the scientific and educational degree "Doctor" in the scientific specialty "Biophysics" in 2007 based on a dissertation on the topic: "Surface properties and behavior of lipid liquid-crystalline phases", and in 2012 he held the academic position of "Associate Professor".

The materials submitted for participation in the competition show the distribution of the scientific assets of Assoc. Prof. Yordanova by points according to the minimum national requirements of the RAS of the Republic of Bulgaria.

As it is clear from the presented documents, the results achieved by Assoc. Prof. Yordanova cover, and in some indicators exceed the requirements set by law.

In group of indicators B (habilitation work) a monograph is presented with the title: Alveolar surfactant - metabolism in norm and pathology. *In vitro* methods for assessing its functional status. Published in 2021 by the University Publishing House "St. Kliment Ohridski".

In group of indicators D (scientific publications in publications that are referenced and indexed in world-famous databases with scientific information) are presented 12 scientific publications that carry 224 points instead required 200. As 3 of them are published in journals with rank Q1, 4 in journals Q2, 3 in Q3 and 2 in Q4. As 10 of the presented works are in journals with IF.

In group of indicators E (citations in scientific journals, monographs, collective volumes and patents) with a minimum national requirement of 100 points, a list of 202 citations is presented, distributed by papers.

In group E, the candidate presented a list of participations in research projects and a list of published university textbooks. Associate Professor Yordanova was the leader of the project DN03 / 16-19.12.2016, funded by the NSF with the amount of BGN 120,000, which is reflected in the report. Impressive is the large number of university and textbooks in which Assoc. Prof. Yordanova is a co-author or lead author. According to this indicator, 150 points are needed, and it is evident from the attached reference that 184.67 points have been collected.

The presented scientific contributions of Assoc. Prof. Albena Yordanova are grouped as follows:

*I. Contributions from the habilitation work (monograph)*

*II. Contributions to scientific papers on indicator G7 (scientific publications in publications that are referenced and indexed in world-famous databases).*

The attached reference presents a habilitation thesis - a monograph on "Alveolar surfactant - normal metabolism and pathology. In vitro methods for assessing its functional status". The monograph describes the mechanisms of development, symptoms and modern therapeutic approaches in the treatment of various lung diseases that occur as a result of lack of "mature" surfactant or its inactivation, under the influence of various factors. It is known that changes in the amount and composition of alveolar surfactant is a major cause of the development of serious pathologies in children and adults, e.g. neonatal respiratory distress syndrome (NDS) in premature infants, acute respiratory distress syndrome in adults, lung cancer, alveolar proteinosis, etc., which can be fatal.

The main contribution of the above-described monograph is the practical orientation. It is shown how to test the functionality of the surfactant with fast, accurate and reliable laboratory in vitro methods, which is crucial not only in newborns, but also in many other diseases - meconium aspiration syndrome, non-small cell lung cancer, alveolar proteinosis, pulmonary pneumonia, allergies, etc. The wider use of clinical probes - gastric aspirates as a reliable, non-invasive and highly informative approach is proposed, which would help neonatologists to quickly resolve therapeutic behavior. The use of adequate tests would be useful in diagnosing and preventing the development of NSAIDs in at-risk infants immediately after birth, as well as predicting the outcome of treatment of affected patients with other respiratory dysfunctions.

*II. The contributions of the scientific papers under indicator G7 (scientific publications in publications that are referenced and indexed in world-famous databases) are presented in subgroups:*

*I.A. Biochemical and biophysical studies of clinical samples from patients to assess the functional status of the lungs in various diseases.*

After a series of biophysical and biochemical experiments, the difference between gastric aspirates of premature and full-term newborns was established. It is shown that the values of surface tension, the shape of the hysteresis curves, the probability of formation of a thin black

film, the morphology of monolayers of gastric aspirates, the expression of different isoforms of individual specific proteins in all studied samples gastric aspirates, depending on the stage of maturation of alveolar surfactant are informative and statistically reliable parameters for rapid assessment of the functional status of alveolar surfactant in neonates with NDS, to be used successfully in clinical practice for rapid assessment of pulmonary maturity and application of exogenous surfactant therapy at risk are important parameters assessment of surfactant maturity in the lung in neonates (publications 55, 70, 77, 78, 80, 81).

It is established from the laboratory analysis of lavage fluids that at each subsequent stage of the procedure the concentrations of proteins and phospholipids decrease and the values of the equilibrium surface tension increase, which confirms the effectiveness of the applied procedure to the cancer patients compared to the control group (publications 63, 64).

#### *I.B. Investigation of intermolecular interactions in model biological membranes through modern highly informative laboratory methods*

It has been found that the presence of hydrophilic polymers prevents the inactivation of alveolar surfactant by plasma proteins by creating an attractive osmotic pressure in the surface film, leading to displacement of unwanted inhibitors from the surface and improving the quality and efficiency of the surfactant and it has been found that the addition of synthetic enkephalin leads to a change in their surface characteristics, which is more pronounced with enkephalinamide. Leucine enkephalins affect the surface characteristics of lipid monolayers and increase their surface density in loose packaging of lipid molecules. This effect is more pronounced with enkephalinamide, which suggests a different mechanism of interaction of amidated enkephalin with the lipid phase compared to leucine-enkephalin. The hypothesis that the electrostatic interactions with the polar lipid heads, the formation of hydrogen bonds between the amino group of ethanolamine and the keto groups in the structure of benzoquinone, as well as the occurrence of hydrophobic interactions between compound B and membrane phospholipids (publications 54, 62, 68, 79).

## II. Contributions of an applied character

### II.A. Biochemical and biophysical studies of clinical samples from patients to assess the functional status of the lungs in various diseases

Analysis of gastric aspirates would limit the application of invasive techniques used so far in clinical practice. A fast and reliable method has been found to determine both the pulmonary maturity of newborns and to assess the functional status of the lungs in patients with respiratory diseases - the hanging drop method (publications 55, 70, 78, 80).

The procedure for conducting complete pulmonary lavage has been optimized, the main contribution being the reduction of the amounts of physiological solution used (from 20 liters to 15 liters) (publications 63, 64).

### *II.B. Investigation of intermolecular interactions in model biological membranes through modern highly informative laboratory methods*

It has been found that when applying hydrophilic polymers, exogenous surfactant preparations reach lower values of the minimum surface tension, and that the combination of the Langmuir monolayer model with Brewster-angle microscopy can be successfully used in preclinical studies for testing the biological activity and the ability to penetrate membranes of newly created analogues of natural analgesics. The use of bacterial-like model membranes helps to reveal the mechanism of the potential antimicrobial action of newly synthesized antibacterial compounds (publications 54, 59, 62, 79).

### *III. Contributions under indicator E 19:*

Textbooks have been developed and published in Bulgarian and English, prepared in accordance with the approved training program in biochemistry for students at the University of Biology and Medicine of Sofia University "St. Kliment Ohridski", collections of theoretical tests and practical tasks from the Regional and National Circles of the Olympiad in Biology and Health Education (publications 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95).

### *IV. Other scientific contributions*

An MDCK cell line expressing hBest1 has been developed that can be used as a suitable model system for studying the functions of human bestrophine. A study was performed to clarify the significance of both the effect of rhamnolipids on lung function. Serum IgG concentrations against *C. pneumoniae* were found to be associated with acute coronary events in smokers and hypertensive patients, gastric aspirates in neonates have been found to have a similar phospholipid composition to tracheal aspirates and are a reliable diagnostic marker for establishing surfactant functionality under gentle conditions (publications 56, 60, 61, 74, 76).

The scientific contributions presented by the candidate correctly reflect the published results. Most of them have an original character. The contributions with applied character are presented separately, as well as the contributions that are related to the pedagogical work of Assoc. Prof. Albena Yordanova.

*In conclusion, I believe that the scientometric indicators presented above, the derived scientific contributions, as well as the overall work of Assoc. Prof. Albena Yordanova fully cover, and in some indicators exceed the requirements for acquiring the academic position "Professor" of the academic staff of the Republic of Bulgaria.*

*My personal impressions of the candidate's work, as well as the duly presented documents on the competition give me reason to confidently recommend to the scientific jury to prepare a proposal to the Faculty Council of the Medical faculty at Sofia University "St. Kliment Ohridski" for the election of Albena Georgieva Yordanova for the academic position "Professor" in the scientific field 4.3 Biological Sciences (Biochemistry).*

15.11.2021

Signature

/Assoc. Prof. B. Nikolova

PhD/