

## OPINION

**from Prof. Sashka Boychova Krumova,**

Member of a scientific committee appointed by order № 684/04.09.2023 of the Director of  
Institute of Biophysics and Biomedical Engineering - BAS,

**Regarding dissertation work for obtaining the educational and scientific degree "PhD",**

in the field of higher education 4. „Natural sciences, mathematics and informatics“,

professional field 4.3. „Biological sciences“,

**scientific specialty „Biophysics“**

**Author of the PhD thesis:** Ariana Anuar Langari

**Topic of the PhD thesis:** „Biophysical characteristics of platelets and erythrocytes in women  
with spontaneous abortions. Markers of disruption of the coagulation system“,

**Scientific supervisor:** Prof. Svetla Jeljazkova Todinova, PhD

The dissertation presented for opinion concerns a common pathology in pregnant women, for which reliable biomarkers for early diagnosis and prevention are still lacking, namely the occurrence of spontaneous abortions. The aim of the dissertation is the establishment of new specific biophysical (morphometric, nanomechanical and thermodynamic) characteristics of erythrocytes and platelets, which are associated with deviations in hemostasis during pregnancy, and could therefore have diagnostic and preventive potential in relation to early loss of the fetus. To achieve the defined goal, 7 relevant scientific tasks are defined and properly executed.

The Introduction of the dissertation defines the current problems in the field and the methodology used. The Literature review presents the basic conditions of hemostasis and the factors that condition it in normal pregnancy, as well as the changes that occur during various pathologies, more specifically in spontaneous abortion. Emphasis is placed on the role of platelets and erythrocytes, the formation mechanisms of these cells, their function in blood coagulation, the composition of the cell membrane and the cytoskeleton, which have a direct relation to the studied biophysical characteristics.



Section "Research objects and used methods" presents in detail the studied groups of patients and controls, as well as the methods and protocols used.

Section "Experimental results and discussion" presents an in-depth study of the defined scientific tasks. The results are presented in 5 tables and 16 original figures. Morphological (shape, roughness) and nanomechanical (elasticity) characteristics of platelets isolated from healthy non-pregnant and pregnant controls and patients with early pregnancy loss (EPL group), as well as coagulation parameters and carrier of thrombophilic factor gene polymorphisms, are investigated. Changes in the morphological and nanomechanical characteristics of platelets were found to correlate with platelet hyperactivation and the carriage of polymorphisms in thrombophilia genes, although the basic coagulation parameters of female patients were not significantly different from those of controls.

The morphometric and nanomechanical characteristics of erythrocytes were also monitored in the same groups of patients/controls, testing freshly isolated cells as well as cells with induced senescence for 40 days. A different pathway of cells ageing in controls and EPL patients was demonstrated, namely strongly reduced membrane elasticity and a faster decrease in plasma membrane roughness in the course of cells senescence for the EPL group. Experiments with stimulated oxidative stress suggest that the antioxidant defense in erythrocytes isolated from EPL patients is weakened or impaired compared to tested controls.

The aging process of erythrocytes was also characterized from a thermodynamic point of view, showing that 71% of EPL patients showed signs of accelerated cell aging, although these patients did not differ from healthy controls in the clinical parameters studied.

The "Summary" section synthesizes the main results in the thesis and their potential to be used as a basis for the development of new protocols for distinguishing pathological complications during pregnancy.

There are 6 clearly defined conclusions, and the parameters that could be used as new diagnostic markers for assessing the risk of spontaneous abortion are identified. The author presents 6 scientific contributions, reflecting the innovation in terms of applied methods and obtained results.

The dissertation is based on 3 publications with a total impact factor of 16.8, in 2 of which Ariana Langari is the first author. Up to this moment, 3 citations are noted.

The doctoral thesis and the scientific achievements of the PhD student are in accordance with and exceed the requirements according to the regulations for the application of the "Law for the development of the academic staff in Bulgaria" and the rules for its application in Institute of Biophysics and Biomedical Engineering – BAS for awarding the educational and



scientific degree "PhD". The narrative summary of the thesis is concise and presents the dissertation work in sufficient detail.

### **Conclusion**

The presented dissertation work and the accompanying materials correspond to and significantly exceed the minimum requirements of the "Law for the development of the academic staff in Bulgaria" and the rules for its application in Institute of Biophysics and Biomedical Engineering – BAS. According to my personal impressions, the PhD student made great efforts in the development of her dissertation work, and a large part of the presented experimental material is her personal contribution.

Based on the above, I confidently give my positive assessment for the presented PhD thesis and suggest to the respected scientific jury to recommend to the Scientific council of Institute of Biophysics and Biomedical Engineering – BAS to award Ariana Anuar Langari the educational and scientific degree "PhD" in professional field 4.3. "Biological Sciences", scientific specialty "Biophysics".

Date: 09.10.2023

Signature:..

/Prof. Sashka Krumova/

