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**REVIEW OF A PH.D. THESIS IN HEALTH AND MEDICAL SCIENCES
IN THE DISCIPLINE OF PHYSICAL CULTURE SCIENCES
WRITTEN BY ZHUO SUN, M.Ed.
TITLED “CORRELATIONS BETWEEN THE GENETIC
VARIANTS IN THE COL22A1, COL27A1, AND COL11A1
GENE AND NON-CONTACT ANTERIOR CRUCIATE
LIGAMENT INJURY IN CAUCASIANS”
WRITTEN AT GDANSK UNIVERSITY OF PHYSICAL EDUCATION AND SPORT
SCIENTIFIC SUPERVISOR: PROF. DR HAB. PAWEŁ CIĘSZCZYK**

Legal Basis for the Review

This scientific dissertation was reviewed on the basis of Resolution No 7 of the Council of the Scientific Committee of the Gdansk University of Physical Education and Sport dated 19 October 2023, under which I have been appointed as the reviewer of the doctoral dissertation by Zhuo Sun, M.Ed., titled Correlations Between the Genetic Variants in the COL22A1, COL27A1, and COL11A1 Gene and Non-Contact Anterior Cruciate Ligament Injury in Caucasians. This appointment was communicated to me by the Chairman of the Scientific Committee, prof. AWFIS dr. hab. Agnieszka Maciejewska-Skrendo.

Relevance of the Topic

In her doctoral thesis, Zhuo Sun, M.Ed. is addressing an important problem regarding damage of the anterior cruciate ligament (ACL), an essential stabilizer in the knee joint, a structure

that is frequently susceptible to contact and non-contact injuries with substantial implications for athletes' performance, physical well-being, and long-term joint health. Studies in this area are important and quite desirable, especially if the high prevalence of this type of injury is taken into account; the incidence in the general population has been estimated at approximately 1 in 3500, which means that about 11,000 to 12,000 ACL ruptures (ACL-R) can be expected every year in the Polish population alone!

It should be noted that scientific literature on this topic is relatively scarce, with only about 60 publications coming up in the search results on PubMed for the keywords “gene polymorphisms ACL injury” and 47 for the phrase “gene polymorphisms athletes ACL injury”, which shows some scientific and practical interest in this subject. However, the findings of those studies are not homogeneous, what suggests that it is desirable and, in fact, necessary to conduct further targeted research in this field. Therefore, the topic presented in this dissertation titled Correlations Between the Genetic Variants in the COL22A1, COL27A1, and COL11A1 Gene and Non-Contact Anterior Cruciate Ligament Injury in Caucasians should be considered as a relevant and scientifically attractive choice.

Formal Evaluation of the Doctoral Thesis

The thesis for the degree of Doctor of Physical Culture written by Ms Zhuo Sun, M.Ed. contains a thematically coherent set of scientific publications, consisting of three papers under the common title Correlations Between the Genetic Variants in the COL22A1, COL27A1, and COL11A1 Gene and Non-Contact Anterior Cruciate Ligament Injury in Caucasians.

The following papers:

(1) Sun Z, Ciężczyk P, Humińska-Lisowska K, Michalowska-Sawczyn M, Yue S. (2023). Genetic Determinants of the Anterior Cruciate Ligament Rupture in Sport: An Up-to-Date Systematic Review. *Journal of Human Kinetics*.

<https://doi.org/10.5114/jhk/163073>

MEiN points value: 140; IF: 2.923

(2) Sun Z, Ciężczyk P, Lulińska E, Dzitkowska-Zabielska M, John M, Humińska-Lisowska K, Michałowska-Sawczyn M, Ficek K, Leońska-Duniec A, Mastalerz A, Janczyk A, & Marek S. (2022). Are COL22A1 Gene Polymorphisms rs11784270 and rs6577958 Associated with

Susceptibility to a Non-Contact Anterior Cruciate Ligament Injury in Po-lish Athletes? International journal of environmental research and public health, 20(1), 515.

<https://doi.org/10.3390/ijerph20010515>

MEiN points value: 140; IF: 4.614

(3) Sun Z, Bojarczuk A, & Cieszczyk P. The COL27A1 and COL11A1 gene variants are not associated with the susceptibility to anterior cruciate ligament rupture in Polish athletes. Balt J Health Phys Act. 2023;15(3).

<https://doi.org/10.29359/BJHPA.15.3.02>

MEiN points value: 70; IF: 0.8

have been attached to the manuscript of the doctoral thesis.

All articles were published in scientific journals with the Impact Factor index, and thus indexed in all bibliographic databases, which fulfils the criteria set by the minister for science. The total score for the presented scientific achievement of Ms Zhuo Sun, M.Ed. in the form of a monothematic series of three scientific publications was, in accordance with the IF and MNiSW scoring system, 8.337 and 350, respectively.

It should be emphasized that all three publications that make up the monothematic set of scientific research papers have a clear biomedical profile. Moreover, the doctoral student is the main author in all the papers and, according to the statements of the other authors, she had “a leading role in the development of the study concept, execution of the experimental part, development and interpretation of the study results and preparation of the manuscript”. The findings are presented in a clear and transparent manner in the form of tables. Moreover, the figures illustrating selected research findings are well-designed and contain all necessary information referred to in the main text.

All studies described and used by the author in her dissertation have been approved by the relevant Bioethical Committee.

Substantive Evaluation of the Doctoral Thesis

Evaluation of a doctoral thesis prepared on the basis of published scientific papers on the main topic requires the reviewer to take a different approach compared to traditional dissertations. After all, the relevant publications in indexed journals have already been thoroughly reviewed by at least two external reviewers, specialists in the field in question, appointed by

the editors of the journals to which those articles had been submitted. Therefore, since the individual papers had already undergone a substantive assessment, it seems important to take a general look at the topic and how it was addressed by the doctoral student across the three publications included in her thesis.

The topic of the doctoral thesis, namely the genetic aspects of non-contact anterior cruciate ligament damage, is very relevant, especially given the statistical data which reveals high prevalence and serious consequences of these injuries for both patients and health insurance funds.

Ms Zhuo Sun, M.Ed. prepared her dissertation based on the form of her scientific achievement, which involves three thematically-related papers published in professional journals. She presented a concise discussion of her scientific achievement in six chapters.

After formally presenting the “List of papers constituting single-subject papers cycle for the PhD dissertation”, the doctoral student moved on to the Introduction.

In this section of the thesis, she introduces the main topic of the series of publications, in which Ms Zhou Sun focused on presenting the whole research spectrum, starting with the role and importance of the entire range of collagens and the pathophysiology of ACL-R, through describing genetic polymorphisms in collagen-encoding genes and genetic variants identified as potential contributors to increased ACL injury risk, to highlighting certain correlations, such as that female athletes are more predisposed to ACL injuries than male athletes.

The issues listed and briefly discussed in the Introduction make a coherent whole, and are adequately supported by the cited literature. She highlights the seriousness of the problem, stating that, considering the increased number, high costs, and detrimental clinical consequences, a deeper understanding of the direct causes and mechanisms is needed to decrease the risk of ACL injury.

The Introduction also shows the reader that there are still many unanswered questions relating to genetic variants associated with anterior cruciate ligament injury. The matter is not made any easier by the available literature, which does not provide clear, unambiguous results and conclusions in many cases. The reason for this is most likely the multifactorial aetiology contributing to ACL damage, especially genetic background (gene polymorphisms), gender, age, training loads, place of residence, diet or comorbidities.

In the next section of the submitted thesis, the doctoral student emphasizes the need to critically approach the results of the available publications and points out the need to carefully analyse all the results in order not to overlook any possible relationships between factors and thus avoid errors in understanding genetic variants' potential association with ACL injuries. It was suggested that specific SNPs—rs11784270 and rs6577958 in the COL22A1 gene, rs946053 in the COL27A1 gene, and rs3753841 in the COL11A1 gene—may contribute to an increased risk of non-contact ACL injuries within the Polish athletic population. It means that these genetic markers might be involved in determining the susceptibility to such injuries.

As with any thesis prepared on the basis of published scientific papers, the doctoral student then briefly discussed all three publications. She highlighted that they included two core experimental papers, both of which utilise a consistent research methodology to examine the central hypothesis, and one systematic review study. She also noted that the thesis investigated the potential genetic predispositions to non-contact Anterior Cruciate Ligament (ACL) injuries, focusing on the Single Nucleotide Polymorphisms (SNPs) within the COL22A1, COL27A1, and COL11A1 genes among Polish athletes. Comprising three studies, the research illuminated the role of genetic factors in the likelihood of ACL injuries.

An important component of Ms Zhou Sun's thesis is a chapter which concerns the "challenges encountered in the current studies and directions for future research". This shows that the doctoral student is an aware and consistent scientist. She also demonstrated a high degree of maturity and logical thinking by neatly organizing the literature in this field, which is not homogeneous, before embarking on her research. She was also able to take a critical look at the research carried out and its limitations, while pointing out the possible impact on the results obtained. This attitude is indicative of a professional approach to scientific work and bodes well for the future.

Summary and Final Conclusion

I consider Ms Zhou Sun's thesis submitted for review to be a valuable and useful study, addressing both scientific and utilitarian aspects of the research problem. The presented findings broaden the scientific knowledge in the field of research on genetic determinants of non-contact anterior cruciate ligament injury. Moreover, she skilfully used the potential of selected research, analytical and statistical tools.

I conclude that this thesis meets all the requirements for a doctoral thesis contained in Article 187 of the Act of 20 July 2018 on Higher Education and Science (consolidated text in Journal of Laws of 2023, item 742). Therefore, I ask the Council of the Scientific Committee of the Gdansk University of Physical Education and Sport to allow Ms Zhou Sun, M.Ed. to proceed with the next stages of proceedings to award the degree of Doctor of Sciences in Physical Culture.

A handwritten signature in black ink, appearing to read 'P. Paweł'.