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To whom it may concern,

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D E C L A R E S ,

That I have read the PhD Thesis manuscript submitted by Mrs. Joanna Zdziennicka of the Department of pre-clinical Veterinary Sciences (Sub-department of pathophysiology) Faculty of Veterinary Medicine, University of Life Sciences in Lublin (Poland).

The thesis: Modifications of the inflammatory response in disorders of musculoskeletal system in animals (Modyfikacje komórkowej odpowiedzi zapalnej w zaburzeniach układu mięśniowo-szkieletowego u zwierząt) deals with a interesting topic in infectology. It has been supervised by Prof. Joanna Wessely-Szponder.

The format of this thesis is a cumulative document of four scientific papers on close related subjects. The immune response has a huge diversity of biological and medical consequences and may involve rejection and failure in transplantation or implant devices, thus such a thesis is pertinent.

The introduction is well written and includes an adequate amount of references. It is enough to acquire a general idea about the topic of the thesis. Then, there is a chapter in which the main methods used are described as well as the materials used. It is also well written and enough to ensure that someone with its content plus that of the papers included after may repeat experiments.

Then the manuscript includes a series of published papers.

Paper 1: It was published in the *Journal of Equine Veterinary Science* (a 1.6 IF and Q2 journal in Veterinary Sciences). The doctoral student was the first author of this paper.

Paper 1 is a clinical/basic job in which the relationship between the activity of neutrophils, the oxidative stress and the injuries in the extremities was clearly demonstrated. This paper also suggested a possible relationship of these conditions and the etiology of osteoarthritis in horses.

Paper 2. It was published in *Microorganisms* (a journal with an IF of 4.128 in Q2 in microbiology). The doctoral student was the first author of this paper. In this paper the authors demonstrate that neutrophil-derived products may generate anti-inflammatory response of macrophages, while other are pro-inflammatory. This paper opens new windows to design innovative therapies to fight different musculoskeletal pathologies.

Paper 3. This paper was published in *Animals* (a journal with an IF of 2.752 and in Q1 veterinary sciences and Q1 in agricultural sciences). The doctoral student was the first author of this paper. In this paper similar studies than in the preceding ones were performed although in this case titanium implantation was used as a model. This is particularly relevant since most of the prosthesis used in traumatology and dentistry are made with titanium. Again the conclusion was that the use of neutrophil-derived products may be useful in diminishing the rates of rejection and failures.

Paper 4. This paper was published in *International Journal of Molecular Sciences* (a journal with an IF of 5.924 and in Q1 in the highly competitive field of Biochemistry & Molecular Biology, and Q2 in Multidisciplinary Chemistry). Again the doctoral student was the first author of the paper. Here a n interesting experimental work was done to show up to which point in long periods of time the interactions between neutrophils, implants and platelets may underlie the final output.

In summary this is an excellent PhD thesis. The scientific production has been brilliant and the accumulated impact factor is 14,404 and the doctorate student has been the first author in all cases.

In my opinion a PhD Thesis should have two main components, the first and more important one is the formation of the candidate that is going to ensure he/she is going to be able to develop research by him/her- self; the second is the generation of some relevant scientific results. This cumulative thesis ensures both.

Specific comments (in fact suggestions):

- In the second paragraph of introduction an scenario of infection is introduced and lacks some explanation since not only infection leads to inflammation.
- P 13 „Neutrophils are the first population of immune cells to reach the lesion" instead „Neutrophils are a population of cells which first reaching the focus of injury"
- P 13 „vessels" or „blood stream" instead circulation
- P 14 „Deoxyribonucleic" instead „Deoxyribonuclear"
- P 15 „humans" instead „people"
- P 16 „Vertebrate antimicrobial peptides are divided....." instead „Antimicrobial peptides are divided into two main groups:"
- P 16 „kill microbes immediately" instead „immediate killing of microbes"
- P 17 „In the excessive or prolonged inflammation they become overactivated and contribute, among others, to the release of a pro-inflammatory cytokine profile, the increase of ROS generation, the excessive proteolytic enzymes release: collagenase, elastase and undergo massive NETosis. Instead „ In the excessive or prolonged inflammation they become overactivated and contribute, among others, the release of a pro-inflammatory cytokine profile, increased ROS generation, excessive proteolytic enzymes release: collagenase, elastase and undergo massive NETosis"
- P 17 „they are necessaries to cope with existing threat by killing microbe" instead „they are necessary to cope with existing threat by killing of the microbe"
- P 18 „broad spectrum" instead „board spectrum"
- P 19 „Taking into account these aspects and the possibility of modulating.." instead „Taking into account these aspects and possibility of modulate"
- P 19 „such as bone fracture involves the use of metal implants to improve healing and restore tissue integrity „ instead „such as bone fracture is involved in using metal implants to improve healing and restore tissue integrity"
- In the section 4.2 (at the end), a suggestion on the eventual translation to human medicine may be added.
- The rest of the manuscript is based on the four mentioned papers.

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Subsequently without hesitation, I firmly believe that the thesis certainly qualifies Joanna Zdziennicka to present and defend it in order to reach the level of Doctor of Philosophy and, therefore, I recommend the acceptance of the PhD thesis of Joanna Zdziennicka with all honors.

"Podsumowując, stwierdzam, że przedłożona mi do oceny rozprawa doktorska Pani lek. wet. Joanny Zdziennickiej **spełnia** wszystkie ustawowe wymogi i kryteria dla rozprawy doktorskiej określone w artykule 13 Ustawy z dnia 14 marca 2003 roku o stopniach naukowych i tytule naukowym oraz o stopniach i tytule naukowym w zakresie sztuki (Dz. U. nr 65 poz. 595 z późniejszymi zmianami). Zwracam się do Wysokiej Rady Dyscypliny Weterynaria o dopuszczenie pani lek. wet. Joanny Zdziennickiej do dalszych etapów przewodu doktorskiego.

I state therefore that the doctoral dissertation of Joanna Zdziennicka submitted to me, **meets** all the statutory requirements and criteria for a doctoral dissertation specified in Article 13 of the Act of March 14, 2003 on academic degrees and academic title as well as academic degrees and title in the field of art (Journal of Laws No. 65, item 595) as amended). in connection with 179 paragraph. 3 of the Act of July 3, 2018, Regulations introducing the Act - Law on Higher Education and Science (Journal of Laws of August 30, 2018, item 1669). Artykuł 13 Ustawy z dnia 14 marca 2003 roku o stopniach naukowych i tytule naukowym oraz o stopniach i tytule naukowym w zakresie sztuki (Dz. U. nr 65 poz. 595 z późniejszymi zmianami) w zw. z art. 179 ust. 3 ustawy z dnia 3 lipca 2018 r. Przepisy wprowadzające ustawę - Prawo o szkolnictwie wyższym i nauce (Dz. U. z 30 sierpnia 2018 r. poz. 1669).)]

Signed Miguel Viñas

Professor