L-Università ta' Malta

Faculty of Health Sciences
Dept. of Applied Biomedical Science

Rm 417, Biomedical Sciences Building
University of Malta,
Msida MDS 2080
Malta

T +356 99945592
david.saliba@um.edu.mt

Report for Doctoral Thesis entitled: "**The role of keratinocyte-derived small extracellular vesicles in the interaction with the immune system in atopic dermatitis**", by Mr. **Adrian Kobiela MSc.**

In this dissertation the candidate presents important knowledge advancement for the role of keratinocyte released extracellular vesicles in the context of atopic dermatitis. Atopic dermatitis affects 15-20% of children worldwide and through atopic march can lead to further complications later on in life.
The candidate presents a framework of key concepts through a detailed introduction to skin tissue structure, aetiology of atopic dermatitis, the dysregulated immune response in the same and the role of extracellular vesicles in intercellular communication. As rightly pointed out by the candidate, there is a gap in knowledge on the composition of keratinocyte released small extracellular vesicles (sEVs) and whether these interact and modulate immune cell responses.
The overarching aim of this thesis is clear and the objective have been formulated to address the research questions outlined in the introduction. It is, indeed, a herculean task that all objectives have been met.
The methods used in this dissertation elegantly underpin how the interplay between skin-resident pathogens and keratinocyte sEVs impacts immune cell activation in atopic dermatitis. The candidate uses a technique of sequential ultracentrifugation for isolation of sEVs as recommended by the ISEV. Specifically, in a paper published in *Frontiers immunology*, the candidate effectively demonstrates the modulation of keratinocyte sEV glycocalyx by pathogenic *Candida albicans*. An important consequence of this sEV glycan modification is the altered interaction with dendritic cell lectin receptors. In a follow-up paper submitted to the *Journal of Extracellular vesicles*, the candidate demonstrates that keratinocyte sEVs have filaggrin-dependent alteration of the lipid profile which ultimately dampens the CD1a auto-reactive T cell activation. The wide array of cutting edge techniques and big data analyses used throughout the three publications are testament to the high level of research conducted by the candidate and other lab members.
It is abundantly clear that the candidate is capable of interpreting research results in context of the current knowledge in the field and also helps push the boundaries for further investigations.

Recommendation
This is an exceptionally strong PhD thesis with remarkable depth of knowledge created using state of the art techniques which opens up new avenues to explore in future projects. I strongly recommend a **Distinction** award for this thesis considering the candidate fulfils the criteria set by the University of Gdansk of publishing high quality papers in high impact journals.

Yours Sincerely,

Prof. David G. Saliba (PhD Edin.)

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Student Name and Surname:	Adrian Kobiela
Title of Dissertation:	The role of keratinocyte-derived small extracellular vesicles in the interaction with the immune system in atopic dermatitis.
Reviewer's Name	David G. Saliba
Reviewer's Contact Details	*Email*: david.saliba@um.edu.mt *Mobile*: 0035699945592

ABSTRACT	The abstract of this thesis is too long making it difficult for the reader to obtain salient points described in this body of work. It is my opinion that the introduction to the topic in this thesis should be limited to one sentence. This should be followed by a key statement of the problem or lack of knowledge in the field warranting this work. A description of the methodology used to characterise the role of keratinocyte sEVs in Atopic Dermatitis and main findings outlined briefly but conclusively. NB. If this is the style commonly used for PhD thesis at UG then please disregard my suggestion for rewriting the abstract.
INTRODUCTION **AIMS and OBJECTIVES**	The overarching aim of the research project is well defined and further subdivided into clearly described objectives. These objectives were achieved and published in high impact peer reviewed journals, namely *Frontiers in Immunology* and *Journal of Extracellular vesicles*.
LITERATURE REVIEW	The literature is extensive although somewhat too lengthy. Some sections are superfluous at addressing the lack of knowledge highlighted by this thesis and could have been omitted (e.g section 1.4.2.). This would have allowed the candidate to place more emphasis on the role of extracellular vesicles and microbiota in allergic conditions and draw parallels in the atopic march of these with Atopic Dermatitis. A key section was the refreshing criticism of the literature concerning the nomenclature used in the field of EV research. Indeed the candidate adheres to the nomenclature adopted by the ISEV. On the other hand, all three research papers have introductions that are relevant and discuss perspectives relative to the main results and lack of knowledge that would be addressed in the corresponding results section.
METHODS	The selection of methods are appropriate for testing the hypotheses listed in this study. All methods are correctly presented and readers of the articles would be able to repeat the experiments or adopt these in future studies. The array of methods used is undeniably impressive and complementary to address the key objectives set out in these publications.
RESULTS	All results in the attached manuscripts are well presented and statistical analysis of these clearly presented in the respective figure legends.
DISCUSSION	The candidate provides a critical evaluation of the methodological approach and results generated in this study in the context of similar studies whilst clearly displaying independent thinking and evaluation of evidence.