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Evaluation of the doctoral dissertation of

**Mr. Jordan Michael Holl, MSc**

with the title

**“IMMUNOMODULATORY PROPERTIES OF NOVEL  
ABDOMINOPLASTY SKIN- DERIVED ACELLULAR DERMAL  
MATRICES”**

from the

Department of Regenerative Medicine and Immune Regulation  
The Medical University of Bialystok

To the Senate of the Medical University Bialystok,

Chronic ulcerative and hard-healing wounds are a growing medical problem worldwide. Skin substitutes, including acellular dermal matrices (ADMs) have shown beneficial effects in healing processes. However several questions still need to be answered. In his doctoral thesis Mr. Jordan Michael Holl, MSc focused on the effect that different methods of human abdominoplasty skin processing have on the acellular dermal matrix immunogenicity. In addition Mr. Holl evaluated immune-modulatory properties of differentially prepared human abdominoplasty skin-derived acellular dermal matrix. Also he worked on the effects of immune cell on the structure of human abdominoplasty skin derived acellular dermal matrix.

Mr. Holl proposed novel strategies for ADM preparation from human abdominoplasty-derived skin. In his thesis skin was processed using three different decellularization methods,

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including the use of anionic detergent (sodium dodecyl sulfate; SDS, in hADM 1) or a non-ionic detergent (Triton X-100 in hADM 2) or a combination of recombinant trypsin and Triton X-100 (in hADM 3).

Mr. Holl showed in his thesis that similarly sourced but differentially processed hADMs possess distinct immunogenicity. hADM 1 shows no immunogenic effects as evidenced by low T cell proliferation and no significant change in cytokine profile. In contrast, hADMs 2 and 3 show relatively higher immunogenicity. Interestingly hADMs exerted no effect on T cell composition after three-day of coincubation. In addition Mr. Holl observed significant changes in the composition of monocytes, indicating their maturation toward a phenotype possessing anti-inflammatory and pro-angiogenic properties.

This study is of high clinical relevance since the use of SDS-based protocols for the purposes of dermal matrix decellularization allow for the preparation of non-immunogenic scaffolds with high therapeutic potential.

The **Introduction** of Mr. Holl's thesis is clear and informative, and critical for the understanding of the work. There are three well-defined and ambitious goals. In the **Material and Methods** section Mr. Holl listed different labor-intensive methods including T cell proliferation assays, cytokine assays or assessments of monocyte and T cell phenotypes. Statistical analysis was performed using Wilcoxon matched-pairs signed rank test and U-Mann Whitney test. The outcomes are presented in the **Results chapter** in the form of a concise report (also for more details the results sections of the enclosed publication can be seen).

The **conclusions and discussions** are adequate and put the results in the published context.

The following pubmed-indexed publications are part of the thesis

**Holl J**, Pawlukianiec C, Corton Ruiz J, Groth D, Grubczak K, Hady HR, Dadan J, Reszec J, Czaban S, Kowalewski C, Moniuszko M, Eljaszewicz A. Skin Substitute Preparation Method Induces Immunomodulatory Changes in Co-Incubated Cells through Collagen Modification. *Pharmaceutics*. 2021 Dec 15;13(12):2164. doi: 10.3390/pharmaceutics13122164.

**Holl J**, Kowalewski C, Zimek Z, Fiedor P, Kaminski A, Oldak T, Moniuszko M, Eljaszewicz A. Chronic Diabetic Wounds and Their Treatment with Skin Substitutes. *Cells*. 2021 Mar 15;10(3):655. doi: 10.3390/cells10030655.

The total impact factor as first author is 12,9. In addition Mr. Jordan Holl was co-author on the following publications:

Groth D, Poplawska I, Tynecka M, Grubczak K, **Holl J**, Starosz A, Janucik A, Borkowska K, Juchniewicz D, Hady HR, Czaban S, Reszec J, Kaminski A, Czech T, Kowalewski C, Fiedor P, Zimek Z, Lewandowska H, Oldak T,



Moniuszko M, Eljaszewicz A. Abdominoplasty Skin-Based Dressing for Deep Wound Treatment-Evaluation of Different Methods of Preparation on Therapeutic Potential. *Pharmaceutics*. 2021 Dec 8;13(12):2118. doi: 10.3390/pharmaceutics 13122118.

Lewandowska H, Eljaszewicz A, Poplawska I, Tynecka M, Walewska A, Grubczak K, **Holl J**, Razak Hady H, Czaban SL, Reszec J, Przybytniak G, Głuszewski W, Sadło J, Dąbrowska-Gralak M, Kowalewski C, Fiedor P, Oldak T, Kaminski A, Zimek Z, Moniuszko M. Optimization of Novel Human Acellular Dermal Dressing Sterilization for Routine Use in Clinical Practice. *Int J Mol Sci*. 2021 Aug 6;22(16):8467. doi: 10.3390/ijms22168467

Grubczak K, Kretowska-Grunwald A, Groth D, Poplawska I, Eljaszewicz A, Bolkun L, Starosz A, **Holl JM**, Mysliwiec M, Kruszewska J, Wojtukiewicz MZ, Moniuszko M. Differential Response of MDA-MB-231 and MCF-7 Breast Cancer Cells to In Vitro Inhibition with CTLA-4 and PD-1 through Cancer-Immune Cells Modified Interactions. *Cells*. 2021 Aug 10;10(8):2044. doi: 10.3390/cells10082044.

The **general assessment** of the doctoral thesis is highly positive and I recommend the Senate of the Medical University of Białystok to allow Mr. Jordan Michael Holl, MSc to proceed with the further steps of the doctoral title conferment procedure. I also recommend that the doctoral thesis of Mr. Jordan Michael Holl, MSc is worth honorable mention based on the scientific work and the publications as first author in international journals.

Prof. Dr. Jochen Utikal