Summary of Results

Chronic ulcerative and hardly healing wounds are a significant clinical problem worldwide. Despite the development of new treatment strategies, their efficacy is unsatisfactory. One of the proposed methods aims to use an acellular dermal matrix (ADM) of animal or human origin. Notably, the source of the skin, the way it is processing, and the sterilization of the final product may affect the therapeutic effectiveness of ADM. An innovative approach is the use of human skin from living donors harvested from a skin fold obtained during the abdominoplasty procedure. However, the impact of different processing methods on the immunomodulatory properties of the novel human ADMs (hADMs) remains elusive. Therefore, the aim of the study was: 1. to analyze the effect of different methods of human abdominoplasty skin processing on acellular dermal matrix immunogenicity; 2. to evaluate immune-modulatory properties of differentially prepared human abdominoplasty skin-derived acellular dermal matrix; and 3. to evaluate the effects of immune cell on the structure of human abdominoplasty skin-derived acellular dermal matrix.

The skin was processed using three different decellularization methods, 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). Peripheral Blood Mononuclear Cells (PBMC) were isolated from the blood of healthy donors by density gradient centrifugation. Freshly isolated cells were incubated in the presence of the prepared hADM. The immunogenicity of novel dermal matrices was assessed based on a T cell proliferation assay using flow cytometry. The in vitro immunomodulatory potential of the new hADMs was evaluated using the multicolor flow cytometry method and immunoassays. The influence of the immune cells on the collagen structure of the matrices was analyzed with confocal microscopy.

First, I found that differentially prepared matrices possess different immunogenicity. The hADM 1 induced low T cell proliferation without significant changes in the cytokine profile. In contrast, hADM 2 and 3 were characterized by higher immunogenicity than hADM1. Next, the activation and phenotype of T cells and monocytes were assessed. Interestingly, analyzed hADMs did not affect T cell phenotype and composition after 3-day incubation. However, significant changes in

the composition of different monocyte subsets were observed, namely increased maturation towards cells with anti-inflammatory and pro-angiogenic potential. These changes were particularly significant after incubating in the presence of hADM1. Finally, the collagen structure of hADM was examined after incubation with immune cells. I observed collagen IV degradation and its collocation with PBMC.

In conclusion, abdominoplasty skin is suitable for the production of hADM. In addition, using anionic detergent in the processing of abdominoplasty skin allows the manufacturing of hADM with low immunogenicity and immunomodulatory properties, indicating a high therapeutic potential. However, further research is needed to assess the therapeutic utility of hADM 1 in treating chronic and hardly healing wounds.