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EVALUATION OF THE IMMUNOMODULATORY EFFECTS OF ACELLULAR DERMAL MATRICES PREPARED BY VARIOUS METHODS

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Relevance. Diabetes mellitus is a global pandemic, affecting over 425 million people worldwide. Diabetic foot ulcer (DFU) is a common severe complication of diabetes, which often leads to lower limb amputation and increased mortality. Novel and effective treatment methods must be explored due to increasing global prevalence of diabetes and DFUs. Human-derived acellular dermal matrices (hADMs) are a promising treatment for chronic non-healing wounds such as DFUs, with a history of beneficial therapeutic outcomes. Nevertheless, appropriate decellularization methods are required to obtain hADMs with optimal therapeutic properties. Therefore, in this study, we analyzed the immunomodulatory properties of hADMs prepared by different decellularization methods.

Target: to investigate the effect of different hADM decellularization protocols on immune cell immunomodulatory properties.

Materials and methods. Skin from bariatric surgery patients undergoing abdominoplasty was decellularized and prepared using three distinct proprietary chemical and enzymatical methods (hADM-1, -2, -3). Next, density gradient centrifugation-derived peripheral blood mononuclear cells (PBMCs) were co-incubated with hADMs for 24, 48 or 72 hours. Following this period, monocyte phenotype (classical, intermediate, non-classical, Tie-2, CD163) and function (TNF, IL-10) were examined via flow cytometry. Finally, cytokine secretion (IFN γ , IL-1 β , IL-6, TNF, IL-17, IL-10, TGF- β) was analyzed by ELISA in cell supernatants. In all cases, these results were compared to unstimulated control.

Results and their discussion. Here we demonstrate the differential immunomodulatory effects induced by method of preparation, resulting in consistently more inflammatory conditions in the case of hADM-2 and -3. Additionally, we have shown that hADM-1 possesses consistently beneficial immunomodulatory and regenerative characteristics similar to unstimulated PBMCs – especially in regard to macrophage phenotype (CD163 & Tie-2) and inflammatory cytokine secretion. Interestingly, comparable levels of the inflammatory mediators, such as IFN γ , IL-1 β , IL-6, TNF, and IL-17 were found in the supernatants from unstimulated control and hADM-1, while hADM-2 & -3 cultures possessed significantly elevated levels of all analyzed cytokines.

Findings. Here we showed that the hADM preparation differentially affects its immunomodulatory properties. Additionally, we found that preparatory method can induce putatively beneficial therapeutic characteristics of hADMs which may result in better clinical outcomes. Although our dressing (hADM-1) appears as a promising treatment of deep wounds and DFUs, further studies are needed to analyze its effectiveness in wound healing *in vivo*.