# Decellularized dermal matrix-based hydrogels and their potential as immunomodulatory biomaterials

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Decellularization is a process that aims to remove cellular and nuclear components from tissues, while preserving the bioactivity of the extracellular matrix (ECM) and minimizing the immunogenicity. Decellularized ECMs positively influence cell adhesion, proliferation, and differentiation, establishing them as promising biomaterials for tissue regeneration [1]. Recent research has highlighted their potential immunomodulatory effect, including their ability to regulate the crosstalk between macrophages and T cells and influence the polarization of macrophages, which leads to an anti-inflammatory and pro-remodelling response [2]. For example, hydrogels derived from decellularized dermal matrix (dDM) have reported potential immunomodulatory effect , namely the regulation of macrophage phenotypes [3, 4]. Using techniques involving enzymatic digestion and collagen crosslinking, dDMs can be converted into hydrogels that preserve growth factors, bioactive binding sites, and the fundamental structural and functional proteins of the ECM. Moreover, hydrogels have the benefit of being injectable and can be used in defect areas with irregular shapes when compared to three-dimensional porous scaffolds [3].

The aim of this study is to develop an hydrogel matrix derived from decellularized rabbit dermal matrix dRDMs and assess its immunomodulatory capabilities for applications in tissue engineering and regenerative medicine. These dermal matrices (dDMs), mostly consisting of collagen, elastin, fibronectin, and laminin, offer advantages over other decellularized tissues regarding availability and adaptability [1]. In addition, by combining the innate immunomodulatory characteristics of dDMs with the adjustable physical properties of hydrogels, we hypothesize that the developed hydrogel will promote a favorable immune response, potentially enabling an immunomodulatory environment.

dRDM, obtained through a chemical decellularization, will be lyophilized and subsequently processed into hydrogels through a pepsin-mediated digestion, followed by pH neutralization and warming to 37 ºC to induce gelation. Since the immunomodulatory response may be conditioned by the hydrogel synthesis process [2], different collagen crosslinking strategies will be evaluated, including photo, thermal, and chemical approaches. Hydrogel formulations will be characterized in terms of rheological properties, microstructure, biocompatibility, and immune response. Immunological assessment will include analysis of cytokine profiles, macrophages polarization markers and immune-related genes.

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