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Optimization of a Skin Fibrosis Model for Anti-fibrotic Drug Testing

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Skin fibrosis remains a significant clinical challenge due to the ineffectiveness of current therapies. A critical barrier to advancing treatment lies in the scarcity of physiologically relevant, reproducible, cellular in vitro models that reflect the best as possible recapitulate dermal fibrosis. This study aims to optimize an in vitro skin fibrosis model by utilizing dextran sulfate as a macromolecular crowding agent in combination with TGF-β1 or a cocktail of pro-inflammatory cytokines (IL-6, IL-13). The objective is to enhance the efficiency of TGF-β1-induced fibroblast-to-myofibroblast transition (FMT) and better mimic fibrotic disorders' excessive extracellular matrix (ECM) protein deposition characteristic. Human dermal fibroblasts serve as the model system, with FMT efficiency assessed through gene expression profiling and protein-level analyses (Western blot and ELISA). Additionally, metabolic activity and cytotoxicity of the new fibrosis model are evaluated using MTT and LDH assays. Preliminary results indicate that an optimized fibrosis model accelerates ECM protein deposition and enhances αSMA, fibronectin, and collagen expression. This optimized model will be a valuable tool for screening anti-fibrotic compounds and developing targeted therapies.

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