The Implications of 3D Culture Models on Keloid Research: A Systematic Review

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Running Title
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BACKGROUND

Treatment responses to keloid lesions vary greatly between patients due to the heterogeneous nature of the disorder. While animal and 2D cell culture models have improved understanding of the underlying mechanisms, they fail to fully replicate the physiological in vivo environment needed for successful therapeutic translation. Recently, advanced 3D human cell culture models have gained traction to address these gaps.

Existing literature highlights limitations in both traditional and 3D approaches, yet lacks a comprehensive summary comparing their relative strengths and weaknesses for modeling keloidogenesis and personalized treatments.

METHODS

A systematic literature search of PubMed (National Library of Medicine), Embase (Elsevier), and Google Scholar was performed using specific search strategies. The search was limited to original research studies that were peer-reviewed, reported on mechanistic outcomes using 2D and/or 3D in vitro cell culture models, and were published in the English language between January 1, 2016, and March 30, 2026.

(PRELIMINARY) RESULTS

A total of 151 unique citations were identified, of which 36 studies met the inclusion criteria. Research suggests that 3D keloid-fibroblast-endothelial spheroids better recapitulate keloid-associated gene-expression patterns and patient-specific drug-resistance profiles than 2D monolayer culture. ROCK inhibitor effects exert significantly stronger antiproliferative and cell-cycle-arresting effects in 3D keloid-fibroblast spheroids than in conventional 2D monolayers. Conversely, no difference in FAP-α expression was reported between 2D and 3D cell culture models of keloid fibroblasts.

CONCLUSİON

Here, we discuss contrast mechanistic outcomes between 3D and 2D in vitro keloid cell culture models, discuss recent contributions of 3D cell culture methods to keloid research and their emerging role in personalized therapies.