Developing a 3D bio-artificial tissue model for breast capsular contracture

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Introduction

Breast capsular contracture is an unpredictable and difficult complication in implant-based breast reconstruction. There is a paucity of non-surgical treatment options, in part due to the lack of human pre-clinical models for capsular contracture. The objective of this study is to develop a 3D bio-artificial tissue (BAT) model of capsular contracture and test the efficacy of an anti-fibrotic RHAMM function blocking peptide (NPI-110).

Methods

Seven breast capsular tissue samples from seven patients undergoing capsulectomy or implant exchange were collected and classified according to Baker grade. Capsular tissue was sectioned and incubated in DMEM media to allow outgrowth of primary fibroblasts. The FlexCell TissueTrain system was used to create bio-artificial collagen 1 tissue cords. 3×10^5 primary fibroblasts from grade 1 and grade 4 cells were embedded into each cord and contraction measured over 14 days. Contracture was then measured over 14 days with the application of 20uM of peptide NPI-110 on day 0 and then 5uM on days 4 and 8 in grade 1 and grade 3 primary fibroblast-embedded cords.

Results

The BAT model reproduces the increased contractility of grade 4 fibroblasts, which demonstrate ongoing cord contractility over 14 days. Grade 1 and 4 cells contract to 50% of control cords by day 2; however, grade 4 cells demonstrate ongoing contraction until day 14 whereas Grade 1 cells plateau after day 9. Peptide testing did not demonstrate any difference between Grade 1 and Grade 3 cells with or without treatment at any time point.

Conclusions

The bio-artificial tissue model accurately replicates enhanced contractility of grade 4 capsular fibroblasts and presents a robust pre-clinical model with applications in future anti-fibrotic peptide testing and personalized medicine. Future experiments will include optimization of peptide dosing and timing.