Sex as a Biological Variable in Pulmonary Fibroblast Mechanical Responses

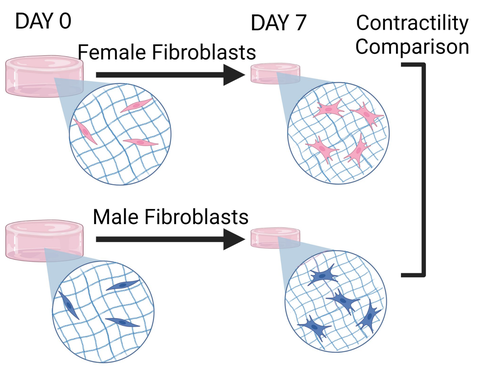
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INTRODUCTION

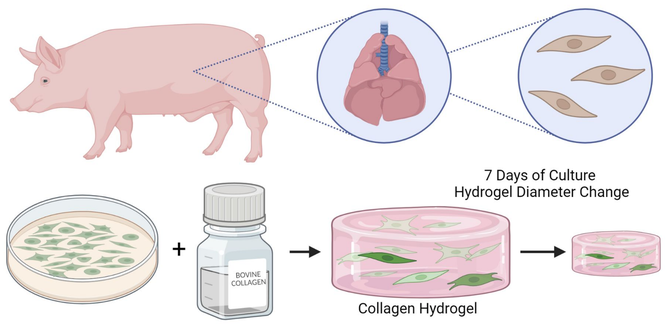
- Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive lung disease characterized by stiff scar formation, leading to shortness of breath [1], [2].
- IPF has a poor prognosis with a median survival of 3 years. Common risk factors for IPF are age and male sex [2].
- IPF is considered a male-dominated disease, but sex as a biological variable in IPF is not yet understood [3].
- Damaged lung tissue causes pulmonary fibroblasts to activate, initiating migration, contraction, and extracellular matrix (ECM) production [1].
- TGF-β1 is a potent growth factor that is overexpressed in the diseased tissue, inducing fibroblast activation and influencing ECM production [4].

PURPOSE STATEMENT

The **purpose** of this study was to assess the influence of sex as a biological variable on fibroblast contractility.



METHODS



- Fibroblast cells were isolated from primary pig lung tissue.
- Fibroblasts were encapsulated in 3D bovine collagen hydrogels.
- Hydrogels were placed in the incubator at 37˚C and 5% CO_2 for 45 minutes to crosslink before being transferred to a 6 well plate.
- TGF-β1 stimulus was performed at 2 ng/mL.
- Hydrogel diameters were measured approximately every 24 hours over 7 days of culture. Gels at a higher cell concentration were measured over 11 hours.

RESULTS

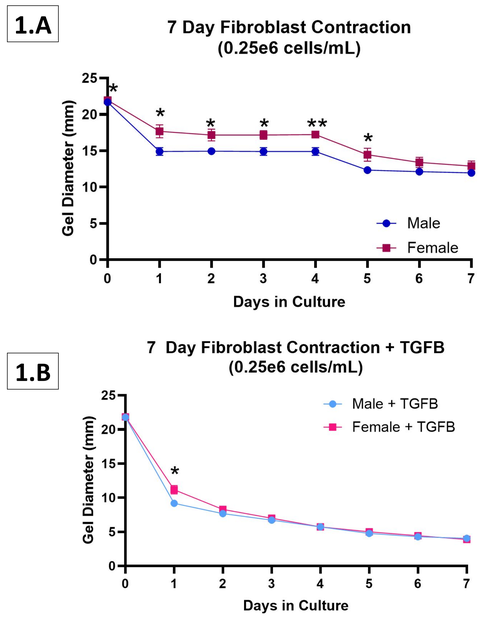


Figure 1. Contraction profiles of fibroblasts under (A) baseline conditions and (B) when subjected to TGF-β1. (**** $p \leq 0.0001$, *** $p \leq 0.001$, ** $p \leq 0.01$, *$p \leq 0.05$)

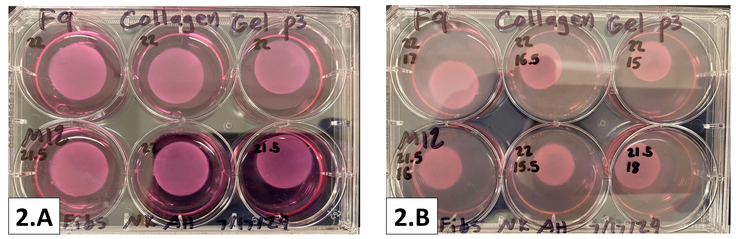


Figure 2. Baseline contraction of male and female hydrogels on (A) day 0 and (B) day 1 of culture.

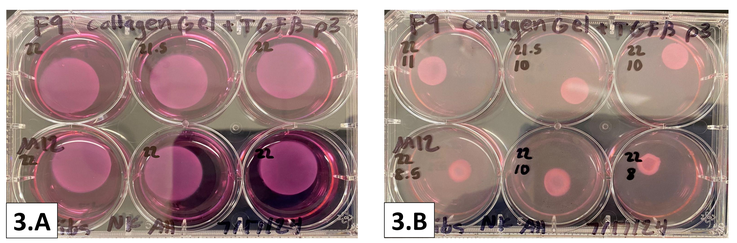


Figure 3. Contraction of male and female hydrogels subjected to TGF-β1 on (A) day 0 and (B) day 1 of culture.

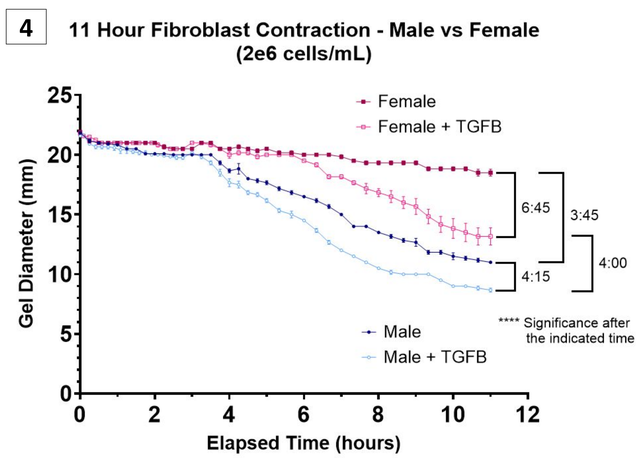


Figure 4. Short term contraction assessment. High cell concentration (2e6 cells/gel) hydrogels were monitored for contraction profiles over 11 hours following gel formation. Significant differences (**** $p \leq 0.0001$) between profiles were found after the indicated time points.

CONCLUSION

- Male fibroblasts are significantly more contractile in 3D.
- Male fibroblasts respond significantly more to TGF-β1 treatment at Day 1 timepoints.

FUTURE DIRECTIONS

- Sex based differences in fibroblast gene expression.
- Sex based differences in cellular morphology.

REFERENCES

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