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The Effect of TGFβ-1 on Adipose-derived Stem Cell (ASC) Ring Constructs

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Biomedical Engineering

Opportunity and Significance

Coronary heart disease (CHD) is the most common type of heart disease.[1] One current method used to address CHD is Coronary Artery Bypass Grafting (CABG). CABG is an effective method, with a 95-98% success rate.[2] However, the procedure could be optimized by eliminating the need for the invasive dissection of a healthy vein or artery and the risk of rejection in the cases with a donor vessel.

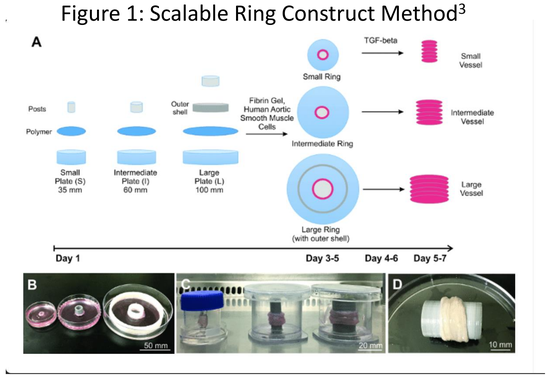
Technical Objectives

Adipose-derived Stem Cells (ASC's) provide an optimal source for potentially graft replacing, tissue-engineered vessel constructs due to their ease of extraction and ability to be patient-specific. In order to make ASC ring constructs a more viable replacement for grafts, they need to have mechanical properties similar to native arteries, which is largely influenced by the extracellular matrix protein collagen. TGFβ-1 is known to stimulate collagen production in ASC's, so this study explores the effect that TGFβ-1 has on the resulting thickness and tensile strength of ASC ring constructs.

Related Work and State of Practice

Dr. Lam's Cardiovascular Regenerative Mechanics Lab has outlined a method with which scalable ring constructs can be formed with polydimethylsiloxane (PDMS) center posts and seeded fibrin hydrogel. This work has been expanded to include 3D-printed inserts as the center posts and has been published in JOVE.[3] Their published work has been done using Smooth Muscle Cells (SMC's). This project uses the scalable ring construct method, shown in Figure 1, with ASC's.

Figure 1: Scalable Ring Construct Method[3]



Method: Ring Construct Seeding, Tensile Testing and Thickness Measurements

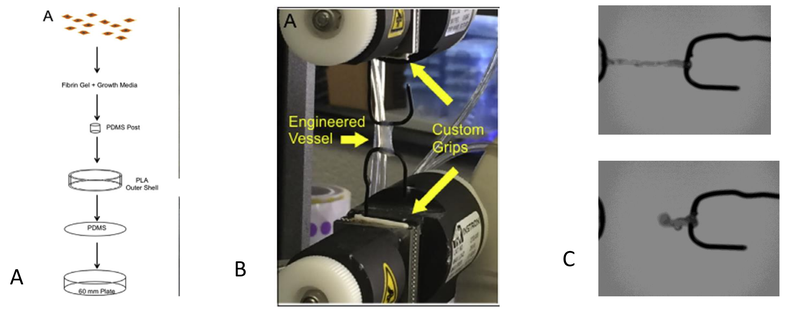
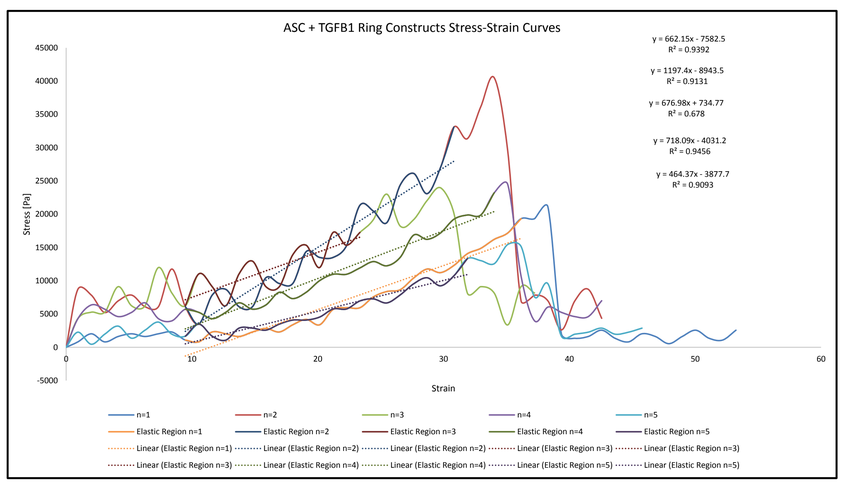


Figure 2: A – Seeding Method[4], 2 million cells seeded, B-- Tensile Test Setup[4], C –Tensile Testing Failure Point

Results: Thickness Measurements and Stress-Strain Curves

Ring Constructs Without TGFβ-1 Avg. Thickness (µm)		
Day 3	Day 5	Day 7
1092.7	885.9	1043.8
1358.4	1215.0	1142.4
912.5	776.2	939.7
1121.2	959.0	1042.0

Ring Constructs With TGFβ-1 Avg. Thickness (µm)		
Day 3	Day 5	Day 7
1556.4	1788.0	1553.0
3202.1	1540.6	1378.8
1790.4	1250.8	1048.7
2183.0	1526.5	1326.8



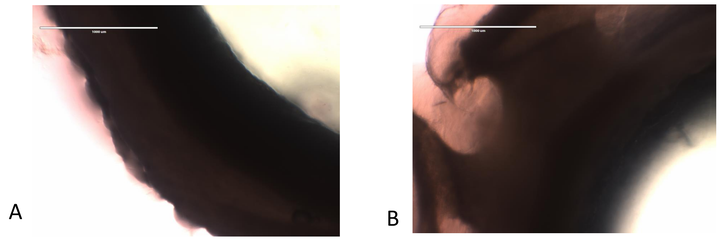


Figure 3: Sample Microscopy Images Taken for Thickness Measurement

Next Steps for Development and Test

In order to make the ring constructs a more viable replacement for grafts, they need to have mechanical properties similar to native arteries. The tensile strength data collected indicates that the ASC rings need to be stronger. The tensile strength of the rings is largely determined by the collagen content of the rings because collagen is an extracellular matrix protein that has high structural properties. Collagen production can also be stimulated in ASC's with the growth factor of Ascorbic Acid (AA). The specific effects of those two growth factors on ASC ring constructs is still unknown. Future development of this project will focus on different iterations of TGFβ-1 and AA and their effect on the mechanical properties and structure of the ASC ring constructs.

Commercialization Plan & Partners

This project was done under the guidance of Dr. Mai T. Lam and her Cardiovascular Regenerative Mechanics Lab. Dr. Lam and her lab will continue to guide the project as it moves forward. The main target consumer for a successful ASC Ring Construct would be a cardiovascular surgeon. Dr. Lam's lab communicates frequently with a cardiovascular surgeon. Moving forward to commercialization, other cardiovascular surgeons would be approached to confirm the handling ability of the rings. Clinical trials would also have to be conducted in order to validate the long-term durability of the ring constructs prior to commercialization.

References

1. "Coronary Artery Disease (CAD)." *Centers for Disease Control and Prevention*. Centers for Disease Control and Prevention, 10 Aug. 2015. Web. 30 Mar. 2017.
2. Hawkes, Anna Louise et al. "Outcomes of Coronary Artery Bypass Graft Surgery." Vascular Health and Risk Management 2.4 (2006): 477–484. Print.
3. Pinnock, Cameron et al. "Scaling of Engineered Vascular Grafts Using 3D Printed Guides and the Ring Stacking Method." JOVE (2017).
4. Pinnock, Cameron et al. "Customizable Engineered Blood Vessels Using 3D Printed Inserts." Elsevier (2015).

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