Thesis Project Portfolio

Peristaltic Pump to Automate Media Flow for Tissue-Engineered Muscle Repair (TEMR) Construct

(Technical Report)

Curbing the Harm of For-Profit Stem Cell Clinics

(STS Research Paper)

An Undergraduate Thesis

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Sociotechnical Synthesis

Volumetric Muscle Loss (VML) injuries occur when a large enough chunk of muscle tissue is lost that the body cannot regenerate it, resulting in loss of function. The Christ lab at the University of Virginia has developed a tissue engineered muscle repair construct (TEMR) to help treat VML consisting of satellite cells – the stem cells which can form new muscle fibers – seeded onto a membrane. Production of this construct includes incubation in a bioreactor which cyclically stretches the membranes to encourage fiber alignment. Due to the 15+ days in incubation, the cell culture media must be changed multiple times by opening the bioreactor. Each new instance of opening the bioreactor is a chance for contamination, ruining the constructs. In addition, this manual media change is labor intensive and inefficient.

To solve this problem, we designed a perfusion system to change media in the bioreactor without the need for human intervention or opening of the bioreactor. We adapted an open source peristaltic pump design to handle higher flow rates before 3D printing the parts, assembling, and calibrating the flow rates. We then optimized the perfusion procedure to prevent bubbles from forming under the membranes while ensuring diffusion of fresh media throughout the bioreactor and minimal waste of media. By pumping a small volume of diluted dye into a water-filled bioreactor , pausing, pumping the same small volume of media out, and pausing again, we could vary flow rate, volume, and pause time. We found that differences in pause time had no significant difference on the amount of dye found in the waste water, which was used as a proxy for wasting fresh media. We successfully implemented a perfusion system which diffuses a half change of media in a closed loop system, and optimized to find parameters that minimize media waste.

The approach the Christ Lab utilizes to create a treatment for VML uses satellite cells, a type of stem cell specific to muscle tissue. Stem cells, which self-renew and can differentiate into more specialized cells, hold enormous promise for medicine. Their ability to differentiate into cell types which divide slowly or not at all has led to efforts to use them to heal wounds, replace lost tissue, or even to create new organs or tissues to be implanted. Although some of these research interests have been able to translate into an FDA approved product that can be used for patients, many have not yet made it to that stage.

The process of designing, testing, and distributing a stem cell product is complex, and the number of groups involved in the development and implementation of these technologies has grown over the past two decades. In 2018, Paul Knoepfler developed a “Stem Cell Ecosystem” model, mapping out the different groups and how they interact. He noted the growth of the ecosystem from 2005-2018 to include a quickly expanding group of for-profit stem cell clinics. These clinics sell unproven stem cell products to patients, often using manipulative tactics and relying on the aura of prestige and validity afforded by study listings on clinicaltrials.gov, IRB approval of studies, and papers published in journals which do little useful peer review. Many instances of adverse effects have been reported in patients who received a stem cell product from for-profit stem cell clinics.

I conducted a literature review on for-profit stem cell clinics, regulatory bodies such as the FDA and Institutional Review Boards, insurance companies, and primary care providers' roles in misinformation mitigation. I primarily focused on exploring and expanding Paul Knoepfler's stem cell ecosystem to include insurance companies and doctors using Actor Network Theory. I then propose potential solutions to mitigate the ability of for-profit stem cell clinics to mislead patients, including more attentive regulation of IRBs and clinics themselves, as well as an education campaign to encourage patients to consult with their primary care provider before receiving a stem cell therapy.